"CLINICAL AND RADIOLOGICAL CORRELATION OF SEVERITY OF ACUTE PANCREATITIS"

A Prospective Study

Dissertation submitted to

THE TAMILNADU Dr. M. G. R. MEDICAL UNIVERSITY

in partial fulfillment of the regulations for the award of the degree of

M. S. GENERAL SURGERY (BRANCH I)

CHENGALPATTU MEDICAL COLLEGE

THE TAMILNADU Dr. M. G. R. MEDICAL UNIVERSITY

CHENNAI, TAMILNADU

MAY 2018

CERTIFICATE

This is to certify that this dissertation titled **"CLINICAL AND RADIOLOGICAL CORRELATION OF SEVERITY OF ACUTE PANCREATITIS"** has been prepared by **DR. PRASHANTH VENKATESAN**, under my supervision in the Department of General Surgery, Chengalpattu Medical College, Chengalpattu, during the academic period 2015 – 2018, and is being submitted to The Tamilnadu Dr. M.G.R. Medical University, Chennai, in partial fulfillment of the University regulation for the award of the Degree "Master Of Surgery" (M. S., General Surgery) and his dissertation is a bonafide work.

Prof.Dr.V.T.ARASU.M.S ,.

PROFESSOR ,
Department of general surgery,
Chengalpattu Medical College ,
Chengalpattu-01

Prof.Dr.RAMULA.M.S, DGO,.

PROFESSOR & HEAD,
Department of general surgery,
Chengalpattu Medical College,
Chengalpattu-01

Prof.Dr.USHA SADASIVAM.M.D.,Ph.D.
DEAN,
Chengalpattu Medical College
Chengalpattu-01

DECLARATION

I, **Dr. PRASHANTH VENKATESAN**, solemnly declare that the dissertation "**CLINICAL AND RADIOLOGICAL CORRELATION OF SEVERITY OF ACUTE PANCREATITIS**" is a bonafide work done by me in the Department of General Surgery, Chengalpattu Medical College, Chengalpattu, Under the able guidance of **Prof. Dr. V.T.ARASU., M.S**, Professor , Department of General Surgery , Chengalpattu Medical College , Chengalpattu .

Place:Chengalpattu **(Dr.Prashanth Venkatesan)**

Date:

INSTITUTIONAL ETHICAL COMMITTEE

CHENGALPATTU MEDICAL COLLEGE, CHENGALPATTU

Title of Work	:	Clinical Radiological Correlation of severity of Acute pancreatitis
Principal Investigator	:	Dr.PrashanthVenkatesan
Designation	:	Post Graduate, Department of General Surgery
Co-Investigators	:	Dr.V.T.Arasu, MS.,
Department	:	Associate Professor, Department of General Surgery, Chengalpattu Medical College, Chengalpattu.

The request for an approval From the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 19.07.2017 at the Medical Education Unit, Government Chengalpattu Medical College, Chengalpattu at 11.00 AM.

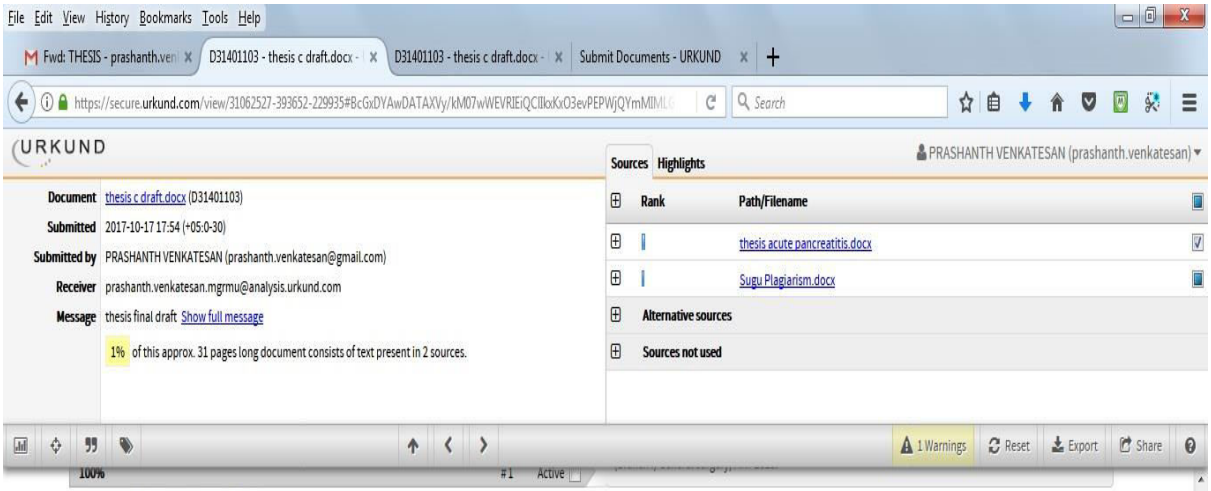
The Members of the committee, the Secretary and the Chairman are pleased to inform you that your proposed project mentioned above is approved.

You should inform the IEC in case of any changes in study procedure, site, investigator investigation or guide or any other changes.

1. You should not deviate from the area of work for which you applied for ethical clearance.
2. You should inform the IEC immediately, in case of any adverse events or serious adverse reactions.
3. You should abide to the rules and regulations of the institution(s).
4. You should complete the work within the specific period and if any extension is required, you should apply for permission again and do the work.
5. You should submit the summary of the work to the ethical committee on complete of work.

MEMBER SECRETARY,
IEC, CHENGALPATTU MEDICAL COLLEGE
CHENGALPATTU.

DEAN
CHENGALPATTU MEDICAL COLLEGE
CHENGALPATTU.



Dr.V.T.Arasu M.S., Dr.Ramula Durai M.S.,

Unit Chief, Head of the Department,

Department of SURGERY, Department of SURGERY, Chengalpattu Medical College Hospital, Chengalpattu Medical College Hospital, Chengalpattu. Chengalpattu.

THE DEAN, Chengalpattu Medical College and Hospital, Chengalpattu.

ACKNOWLEDGEMENT

I am extremely thankful to our beloved unit chief, professor Dr.V.T. Arasu M.S., for granting me permission to conduct this study and for his encouragement, inspiration and guidance to complete this study in Chengalpattu

Medical College Hospital. I am very grateful to our Professor and Head of the Department of surgery, Dr.Ramula Durai M.S., for

her moral support, philosophical guidance and constant support. I am deeply indebted to the Assistant of surgical gastroenterology , Dr.

Senthil Prabhu M.S.,

for his invaluable guidance, perspectives, constructive criticisms throughout the period of study

CERTIFICATE II

This is to certify that this dissertation work titled**" CLINICAL AND RADIOLOGICAL CORRELATION OF SEVERITY OF ACUTE PANCREATITIS''** of the candidate **DR. PRASANTH VENKATESAN** with registration Number 221511253 for the award of degree of M.S. in the branch of **GENERAL SURGERY (BRANCH – I).** I personally verified the urkund.com website for the purpose of plagiarism Check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows 1% percentage of plagiarism in the dissertation.

Guide & Supervisor sign with Seal.

ACKNOWLEDGEMENT

I wish to express my sincere thanks to **Dr.USHA SADASIVAM .M.D.,Ph.D.,** Dean, Chengalpattu Medical College & Hospital, Chengalpattu, for having kindly permitted me to utilize the hospital facilities.

Prof. Dr. RAMULA.M.S,,DGO., Professor & Head of the Department of General surgery, Chengalpattu Medical College & Hospital, Chengalpattu for her immense help, encouragement, guidance and constant support.

I am extremely thankful to our beloved unit chief, professor **Dr.V.T. Arasu M.S.,** for granting me permission to conduct this study and for his encouragement, inspiration and guidance to complete this study in Chengalpattu Medical College Hospital.

I am extremely thankful to **Dr.N.Laxmipathy M.S., Dr.Ganesh Kumar M.S., Dr.Balasubramanaim M.S., Dr.M.Shivan M.S.,** and **Dr.G.Gopinath M.S.,** and other Assistant Professors of surgery for their guidance throughout the study.

I am deeply indebted to the Assistant of surgical gastroenterology , **Dr. Senthil Prabhu M.S.,** for his invaluable guidance, perspectives, constructive criticisms throughout the period of study.

I especially thank my Parents for their technical and emotional support given by them in completing this study.

I also thank my Senior **Dr. Praven Kumar M.S**., for his invaluable

inspiration and guidance to complete this study.

Most importantly I thank my juniors, **Dr. Reka, Dr. Arulvel, Dr. Gokul Prabhu, Dr. Ganesan** for their invaluable help in the ward.

I thank, Professor and Staff of the Department of Radiology for the guidance and permission to utilize their services.

I thank, Professor and Staff of the Department of Biochemistry for the guidance and permission to utilize their services.

I also thank our patients without whom the study would not have been possible.

I owe my thanks to almighty for successful completion of the study.

CONTENTS

LIST OF TABLES

LIST OF GRAPHS

LIST OF ABBREVIATIONS

AP	Acute Pancreatitis
AST	Aspartate Aminotransferase
BISAP	Index Of Severity In Acute Pancreatitis
BUN	Blood Urea Nitrogen
CARS	Counteractive Anti-Inflammatory Response Syndrome
CECT	Contrast Enhanced Computed Tomography
CRP	C-Reactive Protein
CT	Computed Tomography
ERCP	Endoscopic Retrograde Cholangio Pancreato Graphy
FNA	Fine-Needle Aspiration
HLA	Human Leukocyte Antigen
ICAM	Intercellular Adhesion Molecules (ICAM)
IL	Interleukin
LDH	Lactate Dehydrogenase
LPS	Lipopolysaccharide
MHC	Major Histocompatibility Complex (MHC)
MODS	Multiple Organ Dysfunction Syndrome
PAF	Platelet Activating Factor (PAF),
PCT	Procalcitonin
PCT	Procalcitonin
PMN	Polymorphonuclear (PMN)

RCT	Randomized Controlled Trial
SBD	Selective Bowel Decontamination
SIRS	Systemic Inflammatory Response Syndrome
TAP	Trypsinogen Activation Peptide
TNF- A	Tumour Necrosis Factor-A),
URL	Upper Reference Limit
US	Ultrasonography
VARD	Video-Assisted Retroperitoneal Debridement

INTRODUCTION

Acute pancreatitis (AP) is a disease with wide clinical variation, which makes its diagnosis complex. Serum / urinary amylase measurement is a standard diagnostic method, although it was shown to be unable to recognize one fifth of AP patients. The severity of AP forms a continuum, and the average mortality rate approaches 2-10%. Most of the cases are mild and conservative treatment results in a rapid recovery in most of them. However, severe AP constitutes 15–20% of all cases.

In recent decades, mortality rate of severe AP has decreased from 30-80% to 15- 20%. Severe AP is now recognized to be a two-phase systemic disease. In the first phase, extensive pancreatic inflammation and/or necrosis are followed by a systemic inflammatory response syndrome (SIRS) that may lead to multiple organ dysfunction syndrome (MODS) within the first week. About 50% of deaths occur within the first week of the attack, mostly from MODS, which is not different from the systemic complications found in other diseases or injuries (e.g., sepsis, major trauma, burns). Unless the first phase is arrested and reversed by natural defences or therapeutic intervention, the second phase ensues usually after the second week of onset, and includes the formation of infected pancreatic necrosis or fluid collection with possible progression to overt sepsis, MODS and death.

Beger and co-workers showed an overall contamination rate of pancreatic necrosis of 24% within the first week after the onset of AP in patients undergoing surgery for severe AP, increasing to 46% in the second and to 71% in the third week. Organ failure is present only in half of the patients with pancreatic necrosis, and the extent of pancreatic necrosis does not influence the development of remote organ complications.

With an increasing number of failing organ systems involved in AP, the associated mortality rises. The mortality figures associated with MODS vary between 30 and 100%. The association between increasing age and death from AP is well documented. Respiratory failure is the most common type of organ failure in AP. In 719 AP patients, respiratory failure was present in 148 (21%) followed by renal failure in 44 (6%), cardiovascular failure in 28 (4%) and coagulopathy in seven (1%) patients. There is an urgent need to improve the early recognition of patients with severe AP, especially those with subsequent organ failure, so that they can be sent at an early stage to a centre with facilities for maximal intensive care and specialists in endoscopic, radiological and surgical management of AP patients.

Increasing knowledge of the inflammatory process in AP has led to new therapeutic strategies aiming at modifying. The importance of the pro-inflammatory and anti-inflammatory cytokine balance in determining the systemic manifestations and clinical outcome of AP has been emphasized It is necessary to diagnose the systemic inflammatory state of the patient. In an

active pro-inflammatory state, anti-inflammatory therapy may be beneficial. On the other hand, if the patient already has an excessive anti-inflammatory response, Immunosuppressive therapy may be harmful. Moreover, since new immunomodulatory therapies may have undesirable side effects, it is of utmost importance to accurately identify patients who will benefit from immunomodulation.

The purpose of the present investigation was to study the diagnosis and severity assessment of AP. In more detail, the first aim was to evaluate whether diagnosis of AP could be improved. Secondly, inflammatory variables were assessed in predicting severe AP with special reference to subsequent organ failure and radiological parameters were also taken into account. In addition, the mechanisms of the inflammatory cascade and development of immunoparalysis were studied with new cellular markers in AP patients with organ failure.[1]

BACKGROUND:

The first description of the pancreas has been attributed to Herophilus of Chalkaidon about 300 B.C. The naming of this organ, pancreas (Greek: pan, all; kreas, flesh), was not recorded until 400 years later by Rufus of Ephesus (100 A.D.). The earliest case reports of patients dying of suppurative inflammation or tumours of the pancreas were presented by S. Alberti (1578), J. Schenck (1600), and N. Tulp (1641).

The first classification system for AP was reported by Fitz in 1889. In 1901, Opie described the association of gallstones to AP). Alcohol was firmly

established as an important pathogenetic factor in 1917. More than 100 years ago, Chiari (1896) proposed that intra pancreatic activation of zymogens leads to pancreatic auto digestion and is a key factor in the pathogenesis of AP. The association of hyper amylasaemia with AP has been recognized since 1929.

The first report of hereditary AP was from the Mayo Clinic by Comfort and Steinberg. In the history of radiography, the pancreas was a hidden structure seen only indirectly through studies exploring the surrounding organs, such as barium examinations of the upper gastrointestinal tract. Sonography was the first method that permitted direct imaging of the pancreas. Pancreatic imaging essentially developed further with the introduction of computed tomography (CT).

The rationale for surgery in severe AP has evolved over the last 50 years. Initially, total pancreatectomy was often recommended but it resulted in very high mortality rates. The current thinking is that the patients with infected pancreatic necrosis benefit from surgical debridement and drainage of the infected and devitalised tissue. Further, surgery is often necessary if aggressive organ support in an intensive care unit seems inadequate for an AP patient with organ dysfunction.[(2)]

EPIDEMIOLOGY OF ACUTE PANCREATITIS

AP is a common emergency presentation, being responsible for 3% of all hospital admissions with acute abdominal pain The incidence rate of AP varies

considerably in different countries. Low figures have been reported in England (10/100,000) and Germany (15/100,000). In USA, AP affects around 40- 80 per 100,000 of the general population.

In Finland, AP is a common disease, and its incidence has been increasing from 47 to 73 per 100,000 inhabitants/year in 1970-1989, and the increase correlates with alcohol consumption. However, its increased incidence may be partly due to improved diagnostic methods such as CT. [3]

AETIOLOGY OF ACUTE PANCREATITIS

AP has many distinct aetiologies, though approximately 80% of all cases can be attributed to either gallstones or alcohol. The frequency of different forms of AP varies markedly in different countries. Gallstones are the most common cause in the United Kingdom and Asia, whereas in USA and Finland alcohol is the most common causative factor. The idiopathic group still comprises 10-30% of all cases. Increasing interest has been focused on biliary sludge, which has been reported to be present in 70% of AP patients with idiopathic AP. In addition, more than 85 drugs have been reported to cause AP. It has also been recognized that AP can rarely be autosomally dominantly hereditary caused by a mutation in thetrypsinogen-1 gene that allows prematurely activated Trypsinogen to cause acinar cell autodigestion. About 10% of AP cases are associated with other miscellaneous aetiologies. However, although there are various kinds of inducing agents and events, response of the

immune system appears to be identical regardless of the cause. [4]

PATHOGENESIS OF ACUTE PANCREATITIS

PRIMARY EVENTS

The major function of pancreatic acinar cells is the synthesis and secretion of inactive digestive enzyme precursors (Trypsinogen, Chymotrypsinogen, Proelastase, Procarboxypeptidases A and B and Prophospholipase A2) into the duodenum. Zymogens are synthesized in the endoplasmic reticulum and then packaged into secretory granules. Following acinar cell stimulation, the contents of these granules are discharged by exocytosis into the acinar lumen and pass via the pancreatic ductal system into the duodenum, where the conversion of Trypsinogen to Trypsin is catalysed by Enterokinase. Trypsin is the key enzyme for rapid activation of all the Proenzymes, including its own Proenzyme, Trypsinogen. There are two major isoenzymes of Trypsinogen: Trypsinogen-1 and Trypsinogen-2. In healthy subjects, the ratio of Trypsinogen-1 to Trypsinogen-2 in pancreatic fluid is nearly fourfold. Trypsinogen is activated by proteolytic cleavage of a peptide called Trypsinogen activation peptide (TAP). Owing to their potent proteolytic and lipolytic functions, the secretory enzymes represent a considerable degradative (autodigestive) capacity. Compartmental intracellular transport, synthesis of secretory enzymes as inactive zymogens, and the presence of protease inhibitors intracellularly (pancreatic secretory trypsin inhibitor) and in

blood (e.g. alpha-1-antitrypsin and alpha-2 macroglobulin) are major protective mechanisms. The pathogenesis of AP is only partially known.

The initial phase involves triggering events, which are, for the most part, extra-pancreatic in origin. Clinically, the most important of these appears to be either passage of a biliary tract stone or ingestion of ethanol. Although the clinical association of AP with biliary disease and with ethanol ingestion has been firmly established, mechanistic explanations for these associations have proven elusive. In experimental AP, microscopic examination of pancreatic tissue obtained after common bile-pancreatic duct ligation indicates that the earliest signs of cell injury involve acinar cells. The severity of experimental AP has been directly related to the duration of duct obstruction.

Trypsinogen activation, mediated by the lysosomal Hydrolase Cathepsin B within the acinar cells, appears to be an early as well as critical event that leads to cell injury. The disruption of the acinar cell follows after premature activation of the proteases as a result of interaction between the digestive and lysosomal enzymes, and activated proteases then escape into the interstitium of the pancreas. Once released into the pancreatic interstitium, retroperitoneum, peritoneal cavity, and circulation, these enzymes cause necrotizing injury through a variety of events, including local auto digestion by lipase and proteases.

SECONDARY EVENTS:

Pancreatic digestive enzymes explain only part of the pathogenesis of complicated AP. The release of various inflammatory mediators is another important mechanism. In fact, the pathophysiology of severe AP resembles other conditions with SIRS such as sepsis, multitrauma, ischaemia-reperfusion injury and burns, which do not involve the release of digestive enzymes from the pancreas. A pro-inflammatory cytokine cascade follows acinar cell injury. Localized inflammation is the body's initial physiological protective response, which is generally tightly controlled at the site of injury. Loss of this local control results in an excessive uncontrolled activation of inflammatory cells and mediators, which is clinically identified as SIRS. A frequent complication of SIRS is the development of organ system dysfunction, including acute lung injury, shock, renal failure and MODS. The pathogenetic mechanisms leading from localized pancreatic necrosis and inflammation to SIRS with MODS are of particular importance, but these mechanisms are not completely understood.

THE ROLE OF PHAGOCYTE ACTIVATION:

During the last few years it has been recognized that activation of Monocytes / macrophages and polymorphonuclear (PMN) granulocytes is an early event during severe AP and plays an important role in the progression of the disease from a local inflammatory necrosis into SIRS. Leukocyte activation leads to increased leukocyte aggregation and tissue infiltration within the

microcirculation, where these leukocytes (PMNs and macrophages) increase their production of cytokines and other inflammatory mediators, including Prostaglandins, Leukotrienes, Thromboxanes, Platelet Activating Factor (PAF), free radicals, nitric oxide and proteases (Cathepsin, Elastase). Factors released by activated leukocytes, therefore, reflect the severity of the disease. Monocytes have a typical bean-shaped nucleus and are produced in the bone marrow from precursor stem cells. Monocytes migrate into different tissues where they undergo transformation into tissue macrophages with morphological and functional properties that are characteristic of that tissue. In the liver they become Kupffer cells and in the lung, alveolar macrophages.(5)

Monocytes / macrophages carry out the fundamental protective functions of ingesting and killing invading micro-organisms. Macrophages play a central role in the immune response by presenting antigens to lymphocytes during the development of specific immunity. Bacterial endotoxin is a potent activator of mononuclear phagocytes, and it induces the secretion of cytokines involved in host defence and inflammation such as Tumour Necrosis Factor-α (TNF- α), Interleukin (IL) -1, IL-6 and IL-8.

Monocyte activation and increased pro-inflammatory cytokine secretion is associated with the development of systemic complications in AP, and occurs early during the course of the disease. The association suggests that mononuclear phagocyte activation may play an important role in the pathophysiology of organ

failure in these patients.

Excessive stimulation of PMN-granulocytes plays a key role in aggravating AP and contributing to local destruction and systemic complications. Cytokines, such as IL-8, function as chemoattractants and control the movement of PMNs through the extravascular space to the inflammatory site. Once localized, the PMNs ingest and phagocyte particles such as bacteria and immune complexes. Upon activation, the ability of Neutrophils to damage tissues in vivo rests on the formation of free radicals and degranulation of proteolytic enzymes. The most abundant neutral proteolytic enzyme of human Neutrophils is Elastase, which is a specific marker for Neutrophil activation and its plasma concentration is raised early in AP.

Neutrophils mediate tissue-destructive events in a wide range of inflammatory diseases and are especially implicated in the pathogenesis of acute lung injury, which is the most frequently occurring complication in severe AP. The study of Acioli and co- workers has shown evidence for the participation of complement system activation products at an early stage in the priming of Neutrophils and their subsequent entrapment in the lung vasculature during experimental AP. This may be the first step in the development of acute lung injury. PMN has traditionally been thought to participate in the inflammatory response only as an effector cell. However, PMNs can synthesize and release both pro- inflammatory and anti-inflammatory cytokines. Their antagonists hence modulate both the cellular and humoral immunity during the evolution of

the immune response. It seems likely, however, that PMNs have only limited potential as antigen- presenting cells, since they synthesize Major Histocompatibility Complex (MHC) class I but not class II molecules and, therefore, cannot initiate a cellular immune response by presentation of antigen associated with MHC class II to CD4+ T cells.[6]

LEUKOCYTE ADHESION:

Leukocytes, including Neutrophils and Monocytes, the major phagocytes in the bloodstream, circulate in a resting state characterized by low metabolic activity and inability to attach to a normally quiescent vascular endothelium. Leukocytic migration, margination, and adhesion are facilitated by the expression of specific adhesion molecules on both leukocytic and endothelial cell surfaces. Binding to adhesion molecules triggers leukocyte degranulation and generation of free oxygen radicals.

Leukocytic migration into the pancreas is an early and most probably a critical event in severe AP. An influx of leukocytes into the inflamed pancreas has been demonstrated by leukocyte scintigraphy in patients with severe AP. Inflammatory cells infiltrating the interstitial spaces during Caerulein-induced AP include Neutrophils, Monocytes and/or macrophages. Severe AP complicated by acute lung injury is associated with the sequestration of activated inflammatory cells in the pulmonary microvasculature.[7]

SELECTINS:

The role of leukocytes in the inflammatory process is complex and includes rolling along the endothelium, adherence to the endothelium, and trans-endothelial migration into the tissue. A large number of cell surface molecules that are involved in these cell/ endothelium adhesive interactions have been identified and characterized. The initial tethering to and subsequent rolling on the activated endothelium, both reversible events, are mediated by the selectin family of adhesion molecules. The selectin family is composed of three distinct carbohydrate receptors expressed by either endothelial cells (E-selectin), leucocytes (L-selectin) or platelets and endothelium (P-selectin). The selectins and their receptors can exist in a cleaved, soluble form, indicating that they are cleaved or shed from the cell surface by proteases and are measurable in the circulation. Soluble E-selectin (sE-selectin) is an activation marker of the vascular endothelium and the plasma concentrations are increased in patients with SIRS and especially in organ dysfunction and failure. sE-selectin levels are also increased in patients with severe AP. L-selectin is found on the surface of most circulating human Neutrophils, Monocytes, and lymphocytes, and initiates the interaction of these leukocytes to activated endothelium. The measurement of L-selectin expression is difficult, as the expression on cell surface increases and subsequently decreases during leukocyte activation. Therefore, reduced presence of L-selectin on the leukocyte surface may reflect previous leukocyte activation. It is likely that different investigators “catch” the leukocytes at

different stages of activation. The profile of leukocyte L-selectin expression is further affected by the release of L-selectin-rich Neutrophils from bone marrow. However, an inverse relationship between soluble L-selectin and subsequent progression to severe lung injury has been reported. [8]

INTEGRINS:

After leukocyte activation and rolling on the endothelium by means of Selectin expression, the Integrin family regulates the subsequent firm adhesion to activated endothelium. Integrins regulate also leukocyte migration into tissues, their degranulation and phagocytosis. Integrins comprise the largest group of adhesion receptors and are found on most cell types, including leukocytes. The integrins are noncovalent heterodimerscomposed of a family of three α subunits (CD11a, b, and c). The β2 leukocyte Integrins share a common β chain (CD18). CD11b and CD18 combine upon activation, and this complex binds to members of the intercellular adhesion molecules (ICAM) family. Peripheral blood lymphocytes express primarily CD11a/CD18 whereas Neutrophils, Monocytes and natural killer cells express all three β2 Integrins. Intracellular storage pools of CD11b/CD18 and CD11c/CD18 are present in Neutrophils and Monocytes whereas there is no storage pool of CD11a/CD18 (Arnaout 1990). Upon phagocyte activation, additional CD11b/CD18 molecules are rapidly mobilised from intracellular storage granules and expressed on the cell surface. CD11b expression is a marker of Neutrophil activation and likely

vascular transmigration, and increases by multiple stimuli, including bacterial products, cytokines, chemotactic peptides, and lipid mediators. The role of adhesion molecules including measurement of CD11b expression, as determined by flow cytometry, has been extensively studied during the SIRS related to cardiopulmonary bypass surgery and is found to be increased. Increased expression has also been demonstrated in disorders such as sepsis, burn injuries and multitrauma. Importantly, increased CD11b/CD18 expression may predict development of organ failure as has been shown in patients with cirrhosis of the liver and in septic patients. On the contrary, Neutrophils from patients with obstructive jaundice have shown decreased CD11b expression and an impaired response to stimulation with bacterial products, which may lead to high incidence of septic complications in these patients. Upregulation of the adhesion molecule complex CD11b/CD18 has been demonstrated in the pancreatic and lung tissues of rabbits with necrotizing AP. Upregulation of the adhesion molecule in the lungs was associated with marked Neutrophil infiltration, oedema formation and vascular thrombosis, i.e., morphological changes of acute lung injury. Additionally, ICAM-1, the endothelial ligand for the integrin CD11b/CD18, has been shown to be elevated in the serum of patients with severe and in the pancreas and lungs in rats with necrotizing AP. [9]

CYTOKINES:

Considering pro-inflammatory cytokines, SIRS can be categorized in three stages.

Stage 1 is a production of cytokines in response to an injury or infection at the local site of inflammation.

Stage 2 is the protective release of a small amount of cytokines into circulation.

Stage 3 is the failure of homeostasis with the massive systemic reaction where cytokines turn destructive rather than protective. Cytokines are low molecular weight secreted proteins, usually 15-25 kD. They are secreted by many different cell types; the major site of synthesis, however, appears to be cells of the macrophage and Monocyte series.

All cytokines exert their action by binding to specific cell-surface receptors. In an animal model of AP, it has been shown that TNF-α, IL-1, and IL-6 are actually produced also within the pancreatic parenchyma. This is known to occur within an hour of the onset of AP induction and often prior to appreciable changes in pancreatic histology. Most cytokines are not stored as preformed molecules; hence their production requires new gene transcription and translation. In experimental AP it has been demonstrated that TNF-α and IL-1 genes are expressed in the pancreas after induction of AP, resulting in large amounts of intra-pancreatic IL-1 and TNF-α proteins. IL-1 and TNF-α are primary inducers of IL-6 and IL-8 production and are both produced

systemically during AP and not just within the pancreas. Regardless of the animal model used, IL-1 and TNF-α are produced in the spleen, lung, and liver with pancreatic production always preceding that in distant sites by hours or even days, depending on the rapidity of AP development.

In addition to the ability of cytokines to recruit leukocytes to the sites of inflammation, the pro-inflammatory cytokines also induce expression of cell adhesion molecules, both locally and systemically, increase capillary permeability, promote leukocyte adhesion and extravasation, lead to liver acute-phase protein secretion and, thus, play an important role in the systemic manifestations of AP and associated distant organ dysfunction. TNF-α may be one of the chief mediators of inflammation in AP, and the serum concentrations of TNF-α have been shown to correlate to disease severity and systemic complications. However, TNF-α is often undetectable in the sera of patients with AP, even in those with severe disease.

This may be due to the short serum half-life of TNF-α. TNF-α is also broken down by Neutrophil Elastase, which is elevated in patients with severe AP. In septic patients soluble TNF-α receptors may be found in high concentrations in the plasma. Moreover, a stepwise increase in soluble TNF-α receptors with increasing severity of AP has been detected suggesting that the degree of TNF-α-induced inflammation correlates with disease severity. During experimental AP it has been shown that knockout mice lacking receptors for IL-1 or TNF-α have significantly improved survival compared with wild-type animals. In the

cytokine cascade, IL-1 stimulates IL-2, which is produced by T lymphocytes and is principally known as a cytokine responsible for promoting T-cell growth. IL-2 acts by binding to its receptor (IL-2R) expressed mainly on CD4-positive T helper lymphocytes and is considered a marker of T-cell activation. High concentrations of sIL-2R have been shown to predict organ failure in patients with septic shock. Moreover, the level of sIL-2R has been shown to be elevated in patients with severe AP.

IL-6is the principal cytokine mediator of the acute-phase response and is released from Monocytes, macrophages and endothelial cells. IL-6 is often used as a measure for systemic activation of pro-inflammatory cytokines. Prolonged and excessive elevations of circulating IL-6 levels in patients after trauma, burns, and elective surgery have been associated with complications and mortality. Serum levels of IL-6 have also been shown to reflect the severity of an attack of AP, with elevated levels occurring 24-36 h earlier than those of C-reactive protein (CRP).IL-8 is secreted not only by mononuclear phagocytes, but also by other cells, particularly endothelial cells. IL-8 is thought to be the principal secondary mediator of TNF-α-induced Neutrophil activation. IL-8 is a chemotactic agent for Neutrophils and is believed to play a significant role in the development of organ dysfunction and especially sepsis-associated acute lung injury. Indeed, it has been shown that IL-8 is increased in the serum and Broncho Alveolar Lavage fluid in patients with sepsis and severe AP complicated by ARDS. In severe AP, circulating levels of IL-8 appear to closely

parallel IL-6 production. IL-10, the most important anti-inflammatory cytokine is produced by T cells, B cells, Monocytes, and macrophages.

It down-regulates the production of a number of pro-inflammatory cytokines such as IL-1,IL-6 and IL-8, thereby representing a normal endogenous feedback factor of the immune responses and inflammation. In addition, IL- 10 is able to decrease human leukocyte antigen (HLA) -DR expression on Monocytes. IL-10 gene expression correlates with the fall in Monocyte HLA- DR antigen expression in patients undergoing major abdominal surgery and may account for the immunosuppression associated with surgical injury.

The study of Van der Poll and co-workers documented that plasma IL-10 remained high in non- surviving septic patients, while in survivors it significantly decreased during the follow-up. IL-10 has been identified as a mediator that may ameliorate the physiologic consequences of severe AP. [10]

IL-11 is rarely measurable in circulation but has been found to be physiologically active in localized areas of inflammation, such as inflammatory arthritis associated with inflammatory bowel disease. Additionally, IL-11 concentrations have been shown to reflect the severity of AP. IL-13 is produced by activated T cells but not by activated Monocytes. Like IL-10, IL-13 strongly inhibits the secretion of pro-inflammatory cytokines by Monocytes. [11]

PROCALCITONIN*:*

Procalcitonin (PCT) is a polypeptide consisting of 116 amino acids and a molecular size of 13 kDa. It is the precursor protein of the hormone calcitonin. The half-life of PCT in the human body is 25-30 hours. No definitive role is known for PCT before its proteolytic conversion to calcitonin. The exact source of PCT is not known. However, thyroidectomized patients unable to produce calcitonin were shown to possess a calcitonin-like immunoreactivity, thus giving indirect evidence of an extra-thyroidal production. Recently, human liver slices stimulated by TNF-α and IL-6 were detected to produce PCT. Elucidation of the biological role of PCT should contribute to our general understanding of the acute phase reaction. In a recent experimental model of sub-lethal sepsis, PCT appeared to exacerbate mortality after a septic insult, while PCT antiserum attenuated this effect.

Earlier, serum PCT was reported to increase in patients with severe bacterial infections and to correlate with the severity of the infection. It has also been proposed that following cardiac surgery, PCT appears to be useful in discriminating systemic infections from acute phase response or local problems, with simultaneous measurement of CRP increasing the specificity. Recently, there has been increasing evidence that PCT is not only specific for bacterial infection but also an appropriate marker of early development of severe non-infectious SIRS. Raised PCT levels have been reported in other conditions associated with an inflammatory response including trauma, major surgery,

cardiac surgery and heat stroke. Both bacterial pneumonia and non-bacterial pulmonary inflammation caused by inhalational burn injury are associated with a rapid increase in plasma PCT. In trauma patients, the concentration of circulating PCT correlates with the extent of tissue injury and hypovolaemia. Elevated PCT levels have also been reported to predict severe non-infectious SIRS and pulmonary dysfunction secondary to cardiopulmonary bypass. Brunkhorst and co-workers reported that PCT allowed early discrimination between biliary and non-biliary AP, but in subsequent other studies no correlation between PCT concentration and the aetiology of AP has been found. In patients with mild post- ERCP AP, no significant PCT elevation could be observed. Rau and co-workers demonstrated that the degree of PCT elevation reflected the systemic severity of infection in terms of associated organ failure in patients with AP. Müller and co-workers showed PCT to be a valuable variable for differentiating between oedematous and necrotising AP within the first 24 hours of the onset of symptoms, but unlike in the study of Rau and co-workers, PCT was of no value in the early prediction of infected pancreatic necrosis.

CD14:

The Gram-negative bacterial wall consists of inner and outer membranes, the latter of which contains many proteins as well as lipopolysaccharide (LPS) and is chemically unique for each bacterial strain. Endotoxin denotes an impure extract of LPS and various proteins. Endotoxaemia occurs in many patients with

AP. The release is episodic and endotoxin is rapidly cleared from circulation. CD14 is a receptor for LPS and is expressed on macrophages, Monocytes, and Neutrophils. LPS released from gram negative bacteria binds to protein circulating in plasma, which has been found to reflect the severity of AP. The LPS Lipopolysaccharide binding protein complex subsequently binds to the CD14 receptor, triggering cell activation. The causative agents in Gram-positive sepsis are cell-wall components of Gram-positive bacteria, such as Peptidoglycan and Lipoteichoic acid. Like LPS, these bacterial components stimulate excessive release of pro-inflammatory cytokines. Polymorphism in the CD14 receptor causes a genetically determined variation in the reaction of Monocytes / macrophages to infectious stimuli. CD14 modulates the sensitivity of macrophages to LPS, but it does not transmit a signal across the plasma membrane because it lacks an intracellular signaling domain.

Instead, a glycosyl phosphatidylinositol linkage tethers it to the cell surface. Therefore, there is another receptor mediating the signal to the macrophage to secrete cytokines. Five such proteins have been identified in humans and are referred to as toll- like receptors. The gastrointestinal tract is a reservoir of pathogens that may enter the circulation by migrating across the gut mucosal barrier initiating a septic cascade and MODS. Intestinal perfusion is decreased early in haemorrhagic AP.

Gut hypoperfusion may result in increased intestinal permeability. The transmigration of living bacteria or their endotoxins from the gut lumen into the

mesenteric lymph nodes, spleen, peritoneal cavity, and blood, is called bacterial translocation. The translocation of viable bacteria or their endotoxins has been shown to occur in a number of conditions, including haemorrhagic shock, burns, malnutrition, sepsis, jaundice, and AP. However, approximately 50% of patients with multiple organ failure do not have an identifiable focus of infection. Therefore, bacteraemia and endotoxaemia cannot be universal mediators of the syndrome, and other explanations for the pathogenesis of multiple organ failure have been sought. [12]

One proposed explanation is that distant organ injury and failure may be caused by the unfettered synthesis of cytokines by activated macrophages. Moreover, studies on endotoxin resistant mice (i.e., lacking the CD14 molecule) show that the progression of AP, including the production of inflammatory cytokines and early death of the disease, are independent of endotoxin action. [13]

IMMUNOSUPPRESSION

Surgery and traumatic injury often result in a dysregulated hyper-inflammatory response syndrome that may progress to immunosuppression and early MODS. The results of Chenand co-workers and Brivet and co-workers support the hypothesis that, in the early stage of severe AP, activation of various pro-inflammatory and anti-inflammatory cytokines plays an important role in the pathogenesis of the disease. It has also been demonstrated that the

inability to mount an appropriate cytokine (TNF-α or IL-6) response portends a poor prognosis in patients with intra-abdominal sepsis. Thus, immunologic events are believed to be involved in the pathogenesis of AP and they can fluctuate during the course of the disease from a hypersensitive state to immune-paralysis. In an animal model of thermal injury, a relationship between immunosuppression and susceptibility to sepsis has been shown. Similarly, in AP an increased number of infections has been observed in a later stage of the disease presumably as a result, at least partially, of impaired cellular immunity. A decrease in delayed-type skin hypersensitivity reflecting altered cellular immune function is common in patients with burn injury, blunt trauma and after major gastrointestinal surgery, and the decrease correlates with septic morbidity and mortality. Garcia-Sabrido and co-workers were the first to report a correlation between poor outcome and allergy to delayed-type hypersensitivity testing in AP patients. [14]

MONOCYTES:

The initial event in the generation of the specific immune response is the uptake and degradation of foreign antigens by macrophages. The important role of the Monocyte/ macrophage system in the course of poly-trauma and sepsis has been shown in a variety of studies. In immunosupression, these Monocytes are characterized by a markedly reduced HLA-DR expression, and a profound reduction of their ability to produce LPS-induced TNF-α in vitro. Monocyte

HLA-DR expression is of fundamental importance in antigen processing and presentation leading to effective recruitment of a specific immune response. Helper T-lymphocytes require macrophage surface expression of HLADR contiguously in order to initiate a response and to proliferate. The ultimate response is T cell activation and subsequent antibody production by B cells and enhanced phagocytosis of opsonized bacteria. HLA-DR bearing Monocytes therefore play a central role in the generation of the immune cascade. The decrease in HLA-DR expression represents a marker of suppressed immune competence in patients with septic shock and severe thermal injury.

Further, HLA-DR expression on Monocytes is suppressed in traumatized patients with subsequent sepsis and the suppression correlates with the severity of trauma and sepsis as well as with the clinical outcome. The pattern of recovery of HLA-DR on Monocytes may also predict development of septic complications after trauma and infectious complications after elective gastrointestinal surgery. The percentage of peripheral blood Monocytes that express HLA-DR antigen appears to be an accurate marker of the infection associated with immunosuppression. In severe AP, immunoparalysis evidenced by depression of HLA-DR expression of Monocytes, and associated with a persistently high CRP level has been reported to reliably predict a fatal outcome.

Although Monocyte HLA-DR antigen expression correlates clinically with postoperative immunosuppression, the mechanism causing the down-

regulation is unclear. There is circumstantial evidence for the involvement of at least IL-10 in the process of monocytic deactivation in sepsis. Sachse and co-workers demonstrated that in patients with severe burns individual HLA-DR expression and IL-10 were negatively correlated. In vitro, interferon-gamma, IL-4 and granulocyte/macrophage colony-stimulating factor increase Monocyte HLA DR expression, while IL-10, transforming growth factor-beta and prostaglandin-E2 play inhibiting roles. [15]

LYMPHOCYTES:

Along with changes in the Monocyte / macrophage system, a decreased level of total T lymphocytes and especially the proportion of T helper lymphocytes may depress immune function. The study of Curley and co-workers describes immunological abnormalities in AP patients similar to those found in patients with thermal, surgical or traumatic injury. In AP, the concentrations of CD4+ T helper cells correlate with circulating levels of IL-6 and endotoxin as well as disease severity. However, during the first days of severe AP, a decreased lymphocyte count and a strong inverse correlation between the levels of CRP and the proportion of T-helper cells indicating a defective immune response has been reported. Furthermore, in animals with AP, a concomitant reduction in CD4+ T cells with a decreased IL- 2 production has been reported. Similar changes have been observed in humans after thermal and blunt traumatic injury. In contrast, studies show that CD4+ or CD8+ T cells

depleted mice have a significant reduction in the severity of AP, which clearly suggests a pivotal role of T lymphocytes in this disease. [16]

DIAGNOSIS OF ACUTE PANCREATITIS

CLINICAL PRESENTATION

The diagnosis of AP is problematic while there are no specific clinical signs. Patients with AP may suffer from a multitude of symptoms, including upper abdominal pain, meteorism, abdominal resistance, fever, nausea and vomiting, ileus and jaundice. *Abdominal pain* is the major symptom of acute pancreatitis. Pain may vary from a mild discomfort to severe, constant, and incapacitating distress. Characteristically, the pain, which is steady and boring in character, is located in the epigastrium and peri-umbilical region, and may radiate to the back, chest, flanks, and lower abdomen. Nausea, vomiting, and abdominal distention due to gastric and intestinal hypomotility and chemical peritonitis are also frequent complaints.

Physical examination frequently reveals a distressed and anxious patient. Low-grade fever, tachycardia, and hypotension are fairly common. Shock is not unusual and may result from

(1) hypovolemia secondary to exudation of blood and plasma proteins into the retroperitoneal space;

(2) increased formation and release of kinin peptides, which cause vasodilation and increased vascular permeability; and

(3) systemic effects of proteolytic and lipolytic enzymes released into the circulation. Jaundice occurs infrequently; when present, it usually is due to edema of the head of the pancreas with compression of the intra-pancreatic portion of the common bile duct or passage of a biliary stone or sludge. Erythematous skin nodules due to subcutaneous fat necrosis may rarely occur. In 10–20% of patients, there are pulmonary findings, including basilar rales, atelectasis, and pleural effusion, the latter most frequently left sided.

Abdominal tenderness and muscle rigidity are present to a variable degree, but compared with the intense pain, these signs may be less impressive. Bowel sounds are usually diminished or absent. An enlarged pancreas from acute fluid collection, walled off necrosis, or a pseudocyst may be palpable in the upper abdomen later in the course of the disease (i.e., 4–6 weeks). A faint blue discoloration around the umbilicus (Cullen's sign) may occur as the result of hemoperitoneum, and a blue-red-purple or green-brown discoloration of the flanks (Turner's sign) reflects tissue catabolism of hemoglobin from severe necrotizing pancreatitis with hemorrhage.

None of these frequent symptoms are related to the severity of the disease. Rare clinical findings, such as ecchymosis of the flank (Grey Turner sign) or peri-umbilical area (Cullen sign), which occur in 1- 3% of patients, also

fail to effectively predict the severity of AP. Within the first days of admission patients with severe AP may develop SIRS characterized by a combination of fever, tachycardia, and tachypnoea. [17]

LABORATORY DIAGNOSTICS

AMYLASE AND LIPASE

Serum amylase and lipase values threefold or more above normal virtually clinch the diagnosis if gut perforation, ischemia, and infarction are excluded. Serum lipase is the preferred test. However, it should be noted that there is no correlation between the severity of pancreatitis and the degree of serum lipase and amylase elevations. After 3–7 days, even with continuing evidence of pancreatitis, total serum amylase values tend to return toward normal. However, pancreatic isoamylase and lipase levels may remain elevated for 7–14 days. It should be recognized that amylase elevations in serum and urine occur in many conditions other than pancreatitis. Importantly, patients with *academia* (arterial pH ≤7.32) may have spurious elevations in serum amylase. This finding explains why patients with diabetic ketoacidosis may have marked elevations in serum amylase without any other evidence of acute pancreatitis. Serum lipase activity increases in parallel with amylase activity and is more specific than amylase. A serum lipase measurement can be instrumental in differentiating a pancreatic or non-pancreatic cause for hyperamylasemia. *Leukocytosis* (15,000–20,000 leukocytes/μL) occurs frequently. Patients with

more severe disease may show hemoconcentration with hematocrit values >44% and/or prerenal azotemia with a blood urea nitrogen (BUN) level >22 mg/dL resulting from loss of plasma into the retroperitoneal space and peritoneal cavity.

Hemoconcentration may be the harbinger of more severe disease (i.e., pancreatic necrosis), whereas azotemia is a significant risk factor for mortality. *Hyperglycemia* is common and is due to multiple factors, including decreased insulin release, increased glucagon release, and an increased output of adrenal glucocorticoids and catecholamines. *Hypocalcemia*occurs in ~25% of patients, and its pathogenesis is incompletely understood. Although earlier studies suggested that the response of the parathyroid gland to a decrease in serum calcium is impaired, subsequent observations have failed to confirm this phenomenon. Intraperitoneal saponification of calcium by fatty acids in areas of fat necrosis occurs occasionally, with large amounts (up to 6.0 g) dissolved or suspended in ascitic fluid. Such “soap formation” may also be significant in patients with pancreatitis, mild hypocalcemia, and little or no obvious ascites. *Hyperbilirubinemia* (serum bilirubin >68mmoL or >4.0 mg/dL occurs in ~10% of patients. However, jaundice is transient, and serum bilirubin levels return to normal in 4–7 days. Serum alkaline phosphatase and aspartate aminotransferase levels are also transiently elevated, and they parallel serum bilirubin values and may point to gallbladder-related disease or inflammation in the pancreatic head.

Hypertriglyceridemia occurs in 5–10% of patients, and serum amylase levels in these individuals are often spuriously normal. Approximately 5–10% of patients have *hypoxemia* (arterial PO2 ≤60 mmHg), which may herald the onset of ARDS. Finally, the electrocardiogram is occasionally abnormal in acute pancreatitis with ST-segment and T-wave abnormalities simulating myocardial ischemia. An abdominal ultrasound is recommended in the emergency ward as the initial diagnostic imaging modality and is most useful to evaluate for gallstone disease and the pancreatic head. Computed Tomography is used for definitive diagnosis.[18]

TRYPSINOGEN:

Trypsin is the main protease in human pancreatic fluid. It is secreted by the exocrine cells of the pancreas as a proenzyme, Trypsinogen, which is activated in the intestine by Enterokinase. When active trypsin reaches circulation, it is inactivated by the major Trypsin inhibitors in serum, alpha2-macroglobulin and alpha1-antitrypsin. The two major isoenzymes of Trypsinogen are (cationic) trypsinogen-1 and (anionic) trypsinogen-2. In AP, the serum concentrations of trypsinogen-2 are more strongly increased than those of trypsinogen-1. Both the urine and serum trypsinogen-2 measurements and also measurement of the complex trypsin-2- alpha-1-antitrypsin have been shown to be useful markers for AP. Recently, a rapid urinary trypsinogen-2 test strip has proven to accurately identify AP patients in a retrospective study. It,

therefore, appears to be suitable as a screening test for AP.

Other methods: Several assays have been developed to improve the biochemical diagnosis of AP. Serum Elastase stays elevated for up to one week after the onset of AP and may be useful in cases with delayed admission, but the test is not routinely used. Other serum markers such as Ribonuclease, Chymotrypsin, Phospholipase A2 and pancreatic isoamylase have been evaluated, but their use is infrequent because of practical reasons such as long assay times or limited diagnostic advantages over amylase.[19]

RADIOLOGY

Ultrasonography (US) is often utilized for diagnosis of patients with acute abdominal pain. Overlying abdominal gas often limits the ability to image the entire pancreatic gland completely. In AP patients US is important in the evaluation of the gallbladder and the biliary tract to detect possible gallstones and biliary obstruction. US is also useful for follow-up evaluation of a known fluid collection or pseudocyst. Contrast enhanced (CE)-CT has become the standard imaging method in diagnosing and staging AP and its complications. The diagnostic accuracy of CE-CT findings has proved high, reaching a specificity approaching 100%. The use of CT for primary diagnostics is impossible due to limited availability and high costs.[19]

SEVERITY ASSESSMENT OF ACUTE PANCREATITIS

BACKGROUND

Early identification of potentially severe AP is of utmost importance. AP patients with delayed transfer to intensive care have higher mortality to those admitted directly, and mortality even increases when transfer is delayed. There is evidence for benefits of early intensive monitoring and support, enteral feeding, prophylactic antiobiotics and emergency endoscopic sphincterotomy in patients with biliary aetiology in severe AP. One of the main problems with AP has been the lack of accurate predictors of disease severity and the development of organ failure in the early stages of the disease. On admission, clinical assessment of severity has been shown to be unreliable and the severity of AP is independent of the level of serum amylase and lipase. CE-CT has improved the assessment of the disease severity by accurately identifying areas of necrosis. Most investigators define severe AP as a pancreatic necrosis of at least 30% of the gland. It has been reported that necrosis of the head of the pancreas is as dangerous as when the entire pancreas is involved. However, organ failure occurs in only half of the patients with pancreatic necrosis. Magnetic resonance imaging is increasingly used for assessing the severity of AP with quite promising results.

SCORING SYSTEMS

The clinical course of acute pancreatitis is highly unpredictable and may vary from full recovery within a single day to multiorgan failure and mortality within hours or a few days. Although predictive scores initially have been designed to guide clinicians in the initial management and the level of care or observation needed in each patient, their value for day-to-day clinical practice is only limited. The most used scores and cutoff points are listed below

TABLE NO. 1 CLINICAL SEVERITY SCORING SYSTEMS

Predictive Score	Cutoff
APACHE II	≥8 in first 24 hours
BISAP	≥3 in first 24 hours
Modified Glasgow (or Imrie)	≥3 in first 48 hours
Ranson	≥3 in first 48 hours
Urea at admission	>60 mmol/L
C-reactive protein	>150 U/L in first 72 hours

APACHE, Acute Physiology and Chronic Health Evaluation; *BISAP*, bedside index for severity in acute pancreatitis.

TABLE No. 2 a. APACHE II

The APACHE II Severity of Disease Classification System

Physiologic Variable		+4	+3	+2	+1	0	+1	+2	+3	+4
Temperature - rectal (°C)		≥41	39-40.9		38.5-38.9	36-38.4	34-35.9	32-33.9	30-31.9	≤29.9
Mean Arterial Pressure (mm Hg)		≥160	130-159	110-129		70-109		50-69		≤49
Heart Rate		≥180	140-179	110-139		70-109		55-69	40-54	≤39
Respiratory Rate (nonventilated or ventilated)		≥50	35-49		25-34	12-24	10-11	6-9		≤5
Oxygenation (mmHg) a. $FiO_2 > 0,5$ use A-aDO_2 b. $FiO_2 < 0,5$ use PaO_2	a	≥500	350-499	200-349		<200				
	b					> 70	61-70		55-60	<55
Arterial pH		≥7.7	7.6-7.69		7.5-7.59	7.33-7.49		7.25-7.32	7.15-7.24	<7.15
Serum Sodium (mmol/l)		≥180	160-179	155-159	150-154	130-149		120-129	111-119	≤110
Serum Potassium (mmol/l)		≥7	6-6.9		5.5-5.9	3.5-5.4	3-3.4	2.5-2.9		<2.5
Serum Creatinine (mg/dl, Double point score for acute renal failure)		≥3.5	2-3.4	1.5-1.9		0.6-1.4		<0.6		
Hematocrit (%)		≥60		50-59.9	46-49.9	30-45.9		20-29.9		<20
White Blood Count (in 1000/mm³)		≥40		20-39.9	15-19.9	3-14.9		1-2.9		<1
Glasgow-Coma-Scale (GCS)		Score = 15 minus actual GCS								
Serum HCO_3 (venous, mmol/l, use if no ABGs)		≥52	41-51.9		32-40.9	22-31.9		18-21.9	15-17.9	<15
A = Total Acute Physiology Score APS		Sum of the 12 individual variable points								

B = Age Points

≤44 years	0 points
45-54 years	2 points
55-64 years	3 points
65-74 years	5 points
≥75 years	6 points

C = Chronic Health Points

If the patient has a history of severe organ system insufficiency or is immunocompromised assign points as follows:

a. For nonoperative or emergency postoperative patients – 5 points

b. For elective postoperative patients – 2 points

APACHE II Score = Sum of A (APS points) + B (Age points) + C (Chronic Health points)

(From: Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. Crit Care Med 1985;13(10):818-29)

b.Bedside Index of Severity in Acute Pancreatitis (BISAP)Score

- BUN > 25 mg/dL (8.9 mmol/
- Abnormal mental status with a Glasgow coma score <15
- Evidence of SIRS
- > 60 years old
- Pleural effusion

c. Modified Glasgow Score

- PaO2< 7.9kPa
- Age > 55 years
- Neutrophils (WBC > 15)
- Calcium < 2 mmol/L
- Renal function: Urea > 16 mmol/L
- Enzymes LDH > 600IU/L
- Albumin < 32g/L (serum)
- Sugar (blood glucose) > 10 mmol/L

d.Ranson Criteria

On admission:

- Age > 55 years
- Blood glucose>10mmol/l
- WCC > 16 109
- LDH > 350 IU/l
- AST > 250 IU/l

Within 48 hours:

- HCT decrease > 10%
- Serum Urea increase > 0.7 mmol/l
- Serum Ca2+ < 2 mmol/l
- Fluid sequestered > 6 litres
- PaO2 < 8 kPa
- Base deficit > 4 mmol/l

e. Urea > 60 mmol/L

f. C-Reactive protein > 150 U/L

If a patient meets a certain cutoff value, this only means that a patient can at that stage of disease, temporarily, be classified as having "predicted severe

pancreatitis." The clinical value of this label, however, is limited, as the positive predictive value (the chance of truly developing severe pancreatitis) is generally in the order of 50% to70%. Actually, these classifications are most useful in excluding patients at risk for severe pancreatitis, because with a negative predictive value of 85% to 90%, patients with predicted mild pancreatitis run a 10% to15% risk of developing the severe form of the disease.(20)

Acute pancreatitis typically runs a biphasic course. The first phase is characterized by a systemic inflammatory response syndrome (SIRS) and lasts about 2 weeks. The second phase is characterized by a counteractive anti-inflammatory response syndrome (CARS), characterized by a state of immunosuppression. Organ failure in the SIRS phase is considered not to be related to infection but rather to severe systemic inflammation. Organ failure in

the CARS phase is related to secondary infections, such as infected necrosis. Infections, however, do occur in the SIRS phase, but bacteremia and (ventilator-associated) pneumonia are the most prominent types. This was found in a large series of acute pancreatitis patients where it was demonstrated that these infections were most often diagnosed in the first week of admission. Organ failure may affect all organ systems, but the pulmonary and the cardiovascular systems are dominant. The gastrointestinal system also suffers from the state of low flow and SIRS, but signs and symptoms are much more difficult to trace and quantify than oxygen exchange, blood pressure, and urine output. Organ

failure in the SIRS phase is diagnosed at a median of2 days after admission but may already be present at admission. Half of the patients who die from acute pancreatitis suffer from organ failure but not infected necrosis. A recent systematic review of cohort studies demonstrated that 32% of patients who develop organ failure eventually die. Mortality in patients with both organ failure and infected necrosis was 43%.The clinical course of necrotizing pancreatitis is highly variable, and there may be a continuum between the

SIRS and CARS phases. Discrimination into three scenariosis potentially helpful to understand the underlying pathophysiologic processes at hand:

1. Early-onset organ failure (week 1), intensive care admission, followed by improvement with supportive measures and intensive care treatment (weeks 2 through 3). In the weeks to follow (weeks 3 through 5), clinical deterioration occurs. This sequence of events is highly indicative of infection of necrosis.

2. Without early organ failure, clinical stability is suddenly complicated by deterioration in weeks3 through 4 of admission. Again, the chances of infected necrosis as the cause of clinical deterioration are high.

3. Early-onset organ failure does not improve, even after 2 to 3 weeks of supportive treatment in the intensive care unit. In this scenario, a fine-needle aspiration (FNA) of one of the collections has a place to differentiate between persistent SIRS or infected necrosis and to determine the need for intervention.

If, however, gas bubbles are present on CECT scan, no further diagnostic procedures are required, and intervention to treat the source of infection needs to be planned. [20]

TREATMENT

CONSERVATIVE MANAGEMENT

Systemic Inflammatory Response Syndrome Phase

Adequate fluid resuscitation forms the mainstay of initial treatment together with adequate pain relief. A diuresis-guided fluid regimen (goal: 1 mL/kg/hr urine production) is required in the initial phase, as long as organ failure is not present yet. Close monitoring and intravenous fluid supplementation in the initial 24 hours of severe pancreatitis are most important; crystalloid resuscitation volumes as high as 20 L may be required. Unrestricted fluid resuscitation may, however, be harmful. A recent Chinese randomized trial demonstrated that very rapid fluid supplementation aimed at keeping hematocrit levels less than 35% over the first 48 hours was associated with increased mortality. In this phase of the disease, there is no room for intervention (either radiologically, endoscopically, or surgically) for the pancreatic necrosis. Some indications for emergency intervention are discussed later.

Counteractive Anti-inflammatory Response Syndrome Phase and Thereafter If the patient does not improve or deteriorates after initial improvement, infection of pancreatic necrosis and peri-pancreatic collections needs to be ruled out. To anticipate possible further deterioration, some authors advocate weekly FNA of the collection to prove or disprove infection. Many others (including our group) do not support this strategy, because of the possibility of false-negative FNA and the risk of introducing infection. Moreover, in cases of clinical deterioration, a negative FNA should not deter intervention. A recent randomized controlled trial (RCT) that based intervention in patients with necrotizing pancreatitis on clinical grounds rather than on routine FNA indicated that 92% of patients had infected necrosis at the time of initial intervention. Gas bubbles in peri-pancreatic collections are considered pathognomonic for infected necrosis, and FNA is not required.

Prevention Of Infection

As infection is associated with increased mortality in acute pancreatitis, numerous prophylactic strategies have been explored in the past two decades. Enteral bacteria are considered responsible for the majority of these infections, and the current concept is that these bacteria pass through the mucosal barrier in the first 24 hours of disease. In a recent multi-center study of all the infections diagnosed in the course of the disease, the first (usually a bacteremia or

ventilator-associated pneumonia) was diagnosed at a median of 8 days after admission. Infection of necrosis was only diagnosed at a median 26 days.

Mortality from each individual infection (i.e., including pneumonia, bacteremia) was 30%. Bacteremia increased the risk of infection of necrosis from 38% to 65%. In multivariate analysis, persistent organ failure and bacteremia were the strongest predictors of mortality.

Systemic intravenous antibiotics, enteral nutrition, systemic intravenous antibiotics, selective bowel decontamination, and enteral probiotics all have been tried to lower the rate of infection.

Enteral Nutrition

Enteral nutrition is hypothesized to reduce small bowel bacterial overgrowth and to improve intestinal mucosal barrier function, theoretically thereby reducing bacterial translocation and resultant infectious complications. A recent randomized trial has demonstrated that in patients with mild pancreatitis, oral feeding can be started as early as the day of admission or the day thereafter. In predicted severe pancreatitis, it is now generally advised to start enteral nutrition by nasojejunal feeding tube within approximately 3 days, if the patient is not expected to quickly resume a normal diet. A recent meta-analysis demonstrated that in patients with predicted severe pancreatitis, enteral nutrition reduces both infections and mortality compared to the administration

of total parenteral nutrition. There are no clinically relevant differences in outcome between the various enteral nutrition formulations including glutamine supplementation. The optimal route for the administration of enteral feeding through a nasojejunal or a nasogastric feeding tube—has yet to be established. Two relatively small randomized trials including 80 patients found no difference in tolerance for feeding and complication rates. The overall mortality was rather high, and the studies may have failed to show relevant differences in complications, such as aspiration, because of their small size. Results of on going larger studies should be awaited before using nasogastric feeding routinely in patients with severe acute pancreatitis.

Systemic Intravenous Antibiotics

Many studies have addressed the effect of systemic antibiotic prophylaxis in lowering the rate of infectious complications in (predicted) severe acute pancreatitis. The initial, non blinded, non-placebo-controlled, randomized trials showed somewhat positive effects. In the past years, however, three placebo-controlled trials have failed to demonstrate a reduction of infections and/or mortality. A German multi-center trial stressed an increased risk of antibiotic resistance and fungal infections. In a recent analysis, a relationship between methodologic quality and the effect on mortality was documented: “the better the trial the less the positive effect.” A recent updated meta-analysis clearly demonstrated no beneficial effect in the routine use of systemic antibiotic

prophylaxis. So, based on current literature, there is no longer support for the routine prophylactic use of antibiotics.

Selective Bowel Decontamination

If the gut is indeed the source of bacteria responsible for the infectious complications in acute pancreatitis, it might seem a rational approach to administer antibiotic enterally. Many intensive care units nowadays use routine selective bowel decontamination (SBD) or selective oropharyngeal decontamination for a variety of indications. Only one RCT studied the value of SBD in acute pancreatitis and compared the effect of SBD (norfloxacin, colistin, amphotericin) with no SBD in patients with severe acute pancreatitis. A reduction in (corrected)mortality in the SBD group, caused mostly by a reduction of gram-negative infections of pancreatic necrosis, was found. Yet, this study has not been repeated, and the strategy has not gained wide acceptance, but the data suggest that the concept of early intervention in the cascade of events—small bowel bacterial overgrowth, mucosal barrier failure, bacterial translocation, systemic infection—deserves further exploration.

Some placebo-controlled RCTs have shown that prophylactic enteral administration of probiotics is capable of reducing the incidence of infectious complications in pancreas and liver surgery. Two small RCTs from Hungary suggested a beneficial effect of prophylactic use of probiotics in predicted severe pancreatitis. In the large Dutch probiotics trial in patients with predicted

severe acute pancreatitis, however, no effect on infectious complications was found, but a more than twofold higher mortality rate (16% vs. 6%) was shown in the patients receiving probiotics. So far, no satisfactory answer to this puzzling finding has been presented, in spite of several follow-up studies, clinically and experimentally. At this stage, prophylactic probiotics are not recommended for patients with predicted severe acute pancreatitis.

INTERVENTIONAL TREATMENT

Systemic Inflammatory Response Syndrome Phase(First and Second Weeks) Intervention in this phase of the disease should aim at treatment of acute life-threatening complications or prevention of further deterioration. Currently, the only means to prevent deterioration in acute pancreatitis is endoscopic retrograde cholangiopancreatography(ERCP) with sphincterotomy, although its exact place in the therapeutic armamentarium has yet to be established.

The only RCT on surgical necrosectomy in this phase was performed in 1989. In this study, intervention within 72 hours (“early”) was compared with operation after 12days (“late”). The authors terminated this study prematurely because of a much higher, not yet statistically significant, mortality for surgery within 72 hours (58% vs.27%). Based on these findings, early operation to remove necrosis was essentially abandoned. The lessons from the past decades are that in the early phase the clinical picture is dominated by systemic inflammatory responses rather than by the presence or absence of infection of

necrosis. Consequently there is no benefit to be expected from surgical exploration if removal of infected necrosis is the sole indication for exploration.

Indications for Acute Interventions. The only acute complications justifying very early intervention are abdominal compartment syndrome, bowel ischemia or perforation, and severe bleeding unresponsive to angiographic coiling. According to the 2007 international consensus meeting, abdominal compartment syndrome is defined by an intra-abdominal pressure higher than 20 mm Hg with signs of new organ failure. Although the optimal treatment strategy for abdominal compartment syndrome remains to be defined, a consensus meeting suggested that percutaneous drainage can be used as an initial step if intra-abdominal drainable fluid is present. If drainage does not immediately lower the pressure or if there is no (more) drainable fluid, laparotomy for decompression is advised. The pancreas should not be explored because it is too early to remove necrosis safely, and there is a risk to introduce infection into the necrosis. Percutaneous drainage of non-infected collections is not indicated as sterile collections may become iatrogenically contaminated by the percutaneous drains. A recent randomized study, actually advocating the strategy of draining sterile collections, reported on a significant increase in infected necrosis caused by the practice of routine drainage.[21]

Intervention to Prevent Further Deterioration: Early Endoscopic

Retrograde Cholangiopancreatography and Sphincterotomy in Biliary Pancreatitis. The current concept of the etiopathogenesis of acute biliary pancreatitis is that a gallstone, released from the gallbladder into the common bile duct, causes temporary obstruction at the level of the papilla of Vater, leading to obstruction of the pancreatic duct with obstructed flow of pancreatic juice and secondary damage to the exocrine cells with autodigestion of the exocrine pancreas. Theoretically, early relief by ERCP with endoscopic biliary sphincterotomy may stop this process at an early phase and reduce the risk of progression to complications. However, a recent meta-analysis is concluded that there is no benefit of routine ERCP inpatients with predicted severe biliary pancreatitis in the absence of cholangitis. A recent prospective multi-center study demonstrated that ERCP with endoscopic sphincterotomy reduces the complication rate inpatients with predicted severe biliary pancreatitis and cholestasis (arbitrarily defined as bilirubin >2.3 mg/dL[>40 μmol/L] and/or dilated common bile duct).

Intervention in the Second Counteractive Anti-inflammatory Response syndrome Phase:

Intervention for Treatment of Infected Necrosis During the CARS phase or second phase, the patient is threatened by yet another episode of systemic infection or sepsis, caused most often by secondary infection of (peri)pancreatic

necrosis. Documented or suspected infection of pancreatic or peri-pancreatic necrosis with signs of sepsis therefore is the most accepted indication for intervention, radiologically, endoscopically, or surgically. In this phase, less frequent indications for intervention include abdominal compartment syndrome, bleeding, gastric outlet obstruction, common bile duct obstruction, and bowel perforation. Once the threshold for intervention has been reached, the choice is between open laparotomy with necrosectomy and (minimally invasive) surgical, endoscopic, and radiologic percutaneous techniques. The use of these latter techniques is rapidly expanding, but the exact place and indication for any of these three options has not been established.

Timing of Intervention for Infected Necrosis: Third Week and Thereafter Timing and choice of the type of intervention are best guided by an experienced multidisciplinary team. A systematic review of cohort studies concluded that postponing intervention until the intra- and/or extra-pancreatic collections have become encapsulated, a process that usually takes 4 weeks, is beneficial. Such encapsulated collections may be referred to as “walled off necrosis.” In the three clinical scenarios described earlier, encapsulation of the collection may not have been completed, when clinical deterioration occurs. Administration of antibiotics to allow for further encapsulation, under close guidance of the clinical developments and CECT scan, performed at regular intervals to prevent bacteraemia or sepsis, is a valid option to postpone surgical

intervention. In the review mentioned earlier, necrosectomy was performed at a median of 27 days after onset of disease, with a mortality rate of 25%. If intervention was performed in the first 2 weeks, mortality was 75%.Based on the current literature, postponing of intervention, preferably until 4 weeks after onset of disease, is widely accepted as the strategy of choice. The length of the interval is mainly determined by the completeness of encapsulation and the clinical condition of the patient. This policy is obviously only applicable to the subset of patients who survive the initial phase of SIRS and develop infection of necrosis with signs of sepsis, in the CARS phase. [22]

TYPES OF INTERVENTION

Catheter Drainage. Catheter drainage is the least invasive technique for treating infected necrosis. This drain can be placed percutaneously through the (left) retroperitoneum or trans-abdominally, but also through the wall of the stomach or duodenum, simply summarized as "transluminal." A recent systematic review suggested that in approximately 55% of patients with necrotizing pancreatitis, percutaneous catheter drainage can be the only intervention needed for cure. In this review, the technical success rate was 99%, the rate of preoperative organ failure was 77%, and the mortality rate was 17%. Accordingly, a multi-center series from the United States and Canada found that 25% of 40 patients with infected necrotizing pancreatitis can be treated with percutaneous drainage only. Finally, a randomized multi-center trial

demonstrated that catheter drainage is feasible in 99%of patients. In patients who do not improve after technically adequate drainage, necrosectomy should be performed as the next step. The percutaneous drain can be used as a roadmap for (minimally invasive) necrosectomy. This two-step approach—drainage as the first step, followed by drain-guided minimally invasive necrosectomy—is called the *step-up approach* and is now considered by many, but not all, experts the standard of care in patients with infected necrosis.

Minimally Invasive Necrosectomy. In the United States and the Netherlands, the most frequently used minimally invasive surgical intervention is the video-assisted retroperitoneal debridement (VARD) procedure. The first step of the procedure consists of the placement of a left-sided percutaneous retroperitoneal drain through the left flank, if the collection can be reached through this route. The patient is placed in a supine position with the left side slightly elevated.

Guided by the drain, a 5 to 7 cm incision is made, and the necrotic collection is opened. The initial pus and necrosis are removed blindly. Next, a 0-degree laparoscope is introduced in order to remove all the necrosis in reach, under direct vision. Only loosely adherent pieces of necrosis are removed to reduce the risk of bleeding. It is not the goal to remove all necrosis. In contrast to purely percutaneous Necrosectomy techniques, VARD allows for the removal of large pieces of necrosis. In general, the more complete the encapsulation, the easier the Necrosectomy can be performed. A video of this procedure is

available at. Following near-complete debridement, two large-bore surgical drains are placed into the empty cavity, one at the deepest point and one more shallow. Postoperatively, the drains are continuously lavaged with increasing amounts (2, 4, then 6 L) of 0.9% saline per day in the first 3 days. In a recent Dutch multi-center randomized controlled trial in patients with documented or suspected infection of necrosis, the minimally invasive step-up approach and primary open Necrosectomy were compared. A significant difference in major complications and costs was observed, all in favor of the step-up approach, and there was no significant difference in mortality.

A purely percutaneous minimally invasive retroperitoneal Necrosectomy using an operating nephroscope has been described by Carter at al from Glasgow and, later, by the group from Liverpool. A recent series by the latter group suggested a decrease in mortality when using this technique compared to historical controls.

Endoscopic Transluminal Necrosectomy. If VARD is technically not feasible because the infected necrosis does not reach far enough left, then endoscopic transluminal/transgastric Necrosectomy may be a viable option. Since the first description of the transgastric approach by Seifert in 2000, this technique has been increasingly adopted by expert endoscopists, usually gastroenterologists. Results are promising, with success rates ranging from 80% to 93% and mortality from 0% to 6%. Controlled studies are needed, as selection bias may

have influenced these results, and in several series the rate of infection of the necrosis was low. The theoretical advantages are that no abdominal incision(s) are required, and consequently, external pancreatic fistula should not occur, because an internal fistula to the stomach is instead created. Incisional hernia, often difficult to treat after open Necrosectomy, is also avoided. The need for repeated, multiple procedures to remove sufficient amounts of necrosis is a distinct disadvantage for the transgastric technique.

Open Necrosectomy. Until the results of the PANTER trial were published, primary open Necrosectomy was considered the reference standard of treatment in patients with infected necrotizing pancreatitis. One of the most frequently used techniques of open Necrosectomy for infected necrosis is laparotomy with placement of a retroperitoneal lavage system after complete Necrosectomy has been performed. In this technique, initially described by Beger, drains are placed in the lesser sacafter Necrosectomy. These drains are continuously lavaged with increasing amounts (2, 4, then 6 L) of saline per day. Lavage may serve a number of purposes such as mechanical debridement, prevention of tube obstruction, and dilution of pancreatic juice, although the precise benefit is speculative. The mortality of this technique is approximately 25%.Another open approach is open Necrosectomy and closed packing. The group from Boston reported an 11%mortality rate in 167 patients. Their transmesenteric technique of open Necrosectomy is depicted in. Necrosis is approached through the

transverse mesocolon and debrided bluntly, with the goal of removing all necrotic tissue and particulate debris. The resulting cavity is then packed with gauze-stuffed Penrose drains that are removed one by one after a week.

Some groups continue to use an open abdomen strategy with regular, planned relaparotomies as a routine every 3 to 5 days. As the mortality of this procedure is approximately 70%, it is advised to use this only as a rescue strategy, when it is technically impossible to close the abdomen.[22]

TABLE NO. 3

TABLE Treatment of Acute Pancreatitis in Various Clinical Scenarios

Clinical Situation	Advice	Exception
	WEEKS 1-2	
Predicted severe pancreatitis	Fluid supplementation based on urine production, enteral nutrition, adequate pain control. Not useful: routine antibiotic prophylaxis antioxidants, and oral probiotics.	
Abdominal compartment syndrome	Decompression laparotomy without accessing the retroperitoneum	Large amounts of intraabdominal fluid. In these cases percutaneous catheter drainage may be used but should lead to immediate clinical improvement.
Sterile necrosis (collections) and multiple organ failure	Treat organ failure. No evidence that necrosectomy and/or drainage of collections will improve outcome. There is evidence that drainage will increase the risk of infection.	Abdominal compartment syndrome, bowel ischemia, bleeding
	WEEK 3 AND THEREAFTER	
Infected necrosis (collections) without or with only partial encapsulation	If possible, postpone intervention using antibiotics	Rapid deterioration without treatable cause
Infected walled-off necrosis (collections)	Intervention according to the "step-up" approach, starting with (retroperitoneal) catheter drainage. If needed, followed by (minimally invasive) necrosectomy.	Lack of experience; if so, transfer the patient to a more experienced center

AIMS OF STUDY

1. To correlate the severity of acute pancreatitis with regard to available biochemical parameters and Competerized Tomography and correlate both.

2. To predict the outcome and to prognosticate acute pancreatitis with regard to CT abdomen.

REVIEW OF LITERATURE

Acute pancreatitis is a relatively common, potentially life-threatening disease. Few patients develop severe acute pancreatitis, defined by organ failure or necrotizing pancreatitis. Severe pancreatitis is associated with a high mortality of 15% to 30%, whereas the mortality of mild pancreatitis is only 0% to 1%. Organ failure is the most important determinant for mortality in acute pancreatitis. Sterile pancreatic necrosis and sterile peri-pancreatic collections can usually be treated conservatively. However, in some of the patients, secondary infection of necrosis occurs, mostly 3 to 4 weeks after the onset of disease. If left untreated, mortality of infected necrosis approaches 100%.

Gaston Mendez, Jr.[23] did a study on the interim assessment of CT in acute pancreatitis. It was a retrospective study for a duration of 9 months with age bar of 29-68 yrs. CT is the most accurate method currently available for distinguishing the modes of spread of acute pancreatitis into adjacent tissue, especially those involving retroperitoneum and to trace the spread involving various fascial boundaries. Unlike ERCP it is non invasive procedure and is patient compliant. 184 patients (ages 29-68 years) were initially opted for the study in which 102 show symptoms pertaining to the illness like abdominal pain, nausea vomiting, elevation of serum amylase, persistent pain, palpable mass were subjected to CT to evaluate complications and spread. 32 had

abnormal CT which showed pancreatic enlargement. 20 patients exhibited phlegmatous mass, 8 developed pseudocyst, 11 developed abcess and 2 showed evidences of pancreatic hemorrhage. 21 had spread to pararenal space out of which 7 had extensions into psoas muscle. 5 patients had involvement of mesocolon and bowel mesentry. The most common complication expected was pseudocyst, phlegmon and pancreatic abscess. And to find the region of spread, lesser sac, posterior pararenal space, psoas muscle and pelvis. Uncommonly, transverse mesocolon, small bowel mesentry. The result was that on basis of this retrospective study we find that CT is the initial diagnostic procedure for a patient with acute pancreatitis because of its ability to delineate the Complications and spread of the disease.

Michael B. Isikoff [24] did a study to co relate the initial CT examinations of patients of acute pancreatitis with clinical follow up, prognostic signs, and complications and death, 83 patients were selected. The length of hospitalization was compared with the severity of initial CT findings which were grouped based on disease severity (Grade A-Grade E). Out of 83, abcesses occurred in 21.6% of the whole group, while 60% of Grade E alone had abcesses. Grade A and B, patients did not have abscess and none died despite the severity. Abscesses were also seen in 80% of patients with six - eight signs and 12.5% with zero to two signs. Early CT examination in patients of acute pancreatitis is in prognostic indicator of morbidity and mortality.

Buchler m and Malfertheiner[25] did a study on the value of biochemical and imaging procedures for the diagnosis and prognosis of acute pancreatitis. It was a prospective study for a period of 14 Days. Measurements of Alpha-1-protease inhibitors, Alpha-2-macroglubulin, Complement C3, C4 and C reactive protein in two groups of patients with acute pancreatitis. GROUP 1 - 13 patients with edematous interstitial pancreatitis. GROUP 2- 22 patients with necrotizing pancreatitis. Diagnosis of acute pancreatitis was made based on signs, symptoms, pancreatic enzymes, imaging and laprotomy in 24 cases with significant differences between serum parameters. Detection rate - 90% for contrast enhanced CT study. 33%- for Ultrasonography. Necrosis rate - 95% for crp and 85% for alpha 2 macroglubulin. The result was that the determination of both CRP and alpha 2 macroglubulin to probably replace CT in the diagnosis of patients with acute pancreatitis.

Walter Wiesner and Lisa Interire[26] used a a modified CT severity index for evaluating acute pancreatic by comparison of patient outcome and inter-observer variability between modified CT Severity index and currently accepted CT severity index. 266 patients diagnosed with acute pancreatitis were selected for a period of 1 yr. 66 had undergone contrast CT. Modified index included assessment of pancreatic inflammation and necrosis and extra-pancreatic complications. The chosen outcome parameters were length of hospital stay, need for surgery or percutaneous intervention, occurrence of infection, organ

failure and death. The outcome was that the modified CT severity index correlated with patient outcome measures equal to the currently accepted CT severity index with similar inter-observer variability.

Thomas Bollen and Vikesh Singh[27] did a comparison between modified CT severity index and CT severity index in the assessing severity of acute pancreatitis. 397 patient were chosen out of which 196 underwent CT. The severity parameters chosen were mortality, organ failure, pancreatic infection, length of ICU stay, length of hospital stay, need for intervention and clinical severity. The outcome was that there were no particular differences were seen between both Ct indices. In fact both indices correlated with the need for intervention and pancreatic infection. Inter-observer variability was excellent.

Michelle Brand and Andrea Gotz[28] did a study on Acute necrotising pancreatitis - laboratory, clinical and imaging findings as predictors of outcome. The objective was to see whether the laboratory and clinical finding during the early phase of disease and morphological finding in Ct in late phase are helpful in predicting outcome. It was a retrospective study. 99 persons were chosen. The variables taken were albumin, Calcium, CRP, WBC count, acute physiology, age and chronic health evaluation. The patient outcome parameters were peri-pancreatic or pancreatic infection, need for intervention, duration of organ failure and duration of hospital stay. The result

was that out of 99 persons, 25 patients had infection (25%), 42 developed organ failure (42%) and 12 died. Out of the many variables chosen, the independent predictors included albumin level, APACHE 2 score and organ failure. Imaging variables were found to be much more string predictors of patient outcome. CECT at the beginning of late phase is a better disease progression predictor.

Owen Connor, Sebastian Williams, Michael Maher[29] did a study on imaging in acute pancreatitis. As the clinical signs and biochemical markers poorly correlate with the severity of acute pancreatitis imaging is required to confirm diagnosis and detect early complications. Imaging is recommended within first 24 hours to diagnose severe form. To improve prognostic value of CT, CTSI (CT severity index) was developed which has 5 grades. Dual phase CT is recommended for haemorrhagic collection. Thin phase CT is used before any intervention. IV contrast is not used as it increases severity of acute pancreatitis. MRI is preferred when there is Iodine allergy, biliary tract pathology. Radiographic signs include sentinel loop sign, colon cut off sign, with pleural fluid, atelectasis suggesting severe form. Ultrasound is of limited use as it cannot detect necrosis. CECT is the modality of choice for diagnosis and staging. Heterogenous pancreatic collection is necrosis unless proved. CT within first 24 hours is falsely reassuring as necrosis takes 24 to 48 hrs to

develop. Necrosis and abscess are most important features of acute Pancreatitis. MRCP may benefit when iodinated contrast is contraindicated.

METHODOLOGY

DURATION OF STUDY : 3 months (2017)

POPULATION TO BE STUDIED: 61

STUDY GROUP : 18 TO 75 Yrs age group.

STUDY SETTING :

Department of General Surgery, Chengalpattu Medical College and Hospital, Chengalpattu

PATIENTS:

61 patients from both sexes who presented with acute pancreatitis to the department of surgical emergency, Chengalpattu medical college during the period July 2017 to September 2017 were included in the study.

DIAGNOSTIC CRITERIA FOR ACUTE PANCREATITIS:

Acute pancreatitis was diagnosed if there were findings consistent with acute pancreatitis and a raised serum amylase above the upper reference limit (URL). This diagnosis was further complemented with trans-abdominal USG and CE-CT. Exclusion of acute pancreatitis in patients with acute abdominal pain was based on clinical, radiographic, endoscopic and surgical findings.

SEVERITY ASSESSMENT OF ACUTE PANCREATITIS:

Assessment of severity based on clinical presentations. Assessment of severity was also based on CT abdomen. A correlation was obtained between clinical severity and that based on CT abdomen.

SCORING SYSTEMS:

CLINICALSCORING:

a. In AP patients appropriate laboratory and physiological data were recorded On day 1 and 48 hours after admission to calculate the Ranson criteria.

RANSONS CRITERIA

On admission

- Age: >55 years
- White blood count: >16 000/mm
- Blood glucose level: >11.0 mmol/L
- Lactate dehydrogenase (LDH): >350 IU/L
- Aspartate aminotransferase (AST): >250 U/L

At 48 hours

- Packed cell volume: decrease >10% from admission
- Urea: increase >1.8 mmol/L from admission equivalent to blood urea nitrogen (BUN): increase >5 mg/dL from admission
- Calcium: <2 mmol/L
- Oxygen partial pressure: <60 mmHg
- Base deficit: >4 mmol/L
- Fluid sequestration: >6 L

Prognosis

- 0-2 criteria: <1% mortality
- 3-4 criteria: 16% mortality
- 5 or more: >40% mortality

b. MODS score provides a means to grade the intensity of dysfunction of six organ systems: the respiratory (spo2), renal (serum creatinine), hepatic (serum bilirubin), nervous system (GCS), cardiovascular(pulse rate) and the hematological system (platelet count).

MODS SCORING

TABLE NO. 4

ORGAN SYSTEMS	0	1	2	3	4
RESPIRATORY Spo2 in %	100	90-100	80-90	70-80	<70
RENAL Serum creatinine in mic.mol/l	<=100	101-200	201-350	351-500	>500
HEPATIC Serum bilirubin in mmol/l	<=20	21-60	61-120	121-240	>240
CARDIOVASCULAR Heart rate in BPM	70-80	81-90	91-100	101-110	110-120
HEMATOLOGICAL Platelet count *10^9	>120	81-120	51-80	21-50	<=20
NEUROLOGICAL GCS	15	13-14	10-12	7-9	<6

0 points:	ICU Mort 0%, Hosp Mort 0%, ICU Stay 2 Days
1-4 points:	ICU Mort 1-2%, Hosp Mort 7%, ICU Stay 3 Days
5-8 points:	ICU Mort 3-5%, Hosp Mort 16%, ICU Stay 6 Days
9-12 points:	ICU Mort 25%, Hosp Mort 50%, ICU Stay 10 Days
3-16 points:	ICU Mort 50%, Hosp Mort 70%, ICU Stay 17 Days
17-20 points:	ICU Mort 75%, Hosp Mort 82%, ICU Stay 21 Days
21-24 points:	ICU Mort 100%, Hospital Mortality 100%

CT SCORING(BALTHAZAR):

TABLE NO. 5

GRADE	APPEARANCE	SCORE
Grade A	Normal appearance	0
Grade B	Focal or diffuse enlargement of pancreas.	1
Grade C	Peri-pancreatic inflammation	2
Grade D	Intra/ extra-pancreatic fluid collection.	3
Grade E	Two or more fluid collection or gas in pancreas or retroperitoneum	4

CT SEVERITY INDEX:

Necrosis score based on CE-CT.

- 0% OF NECROSED PANCREAS : 0
- <33% OF NECROSED PANCREAS : 2
- 33 – 50% OF NECROSED PANCREAS : 4
- >50% OF NECROSED PANCREAS : 6

CT severity index = unenhanced CT score + necrosis score

0-3: Mild Acute Pancreatitis

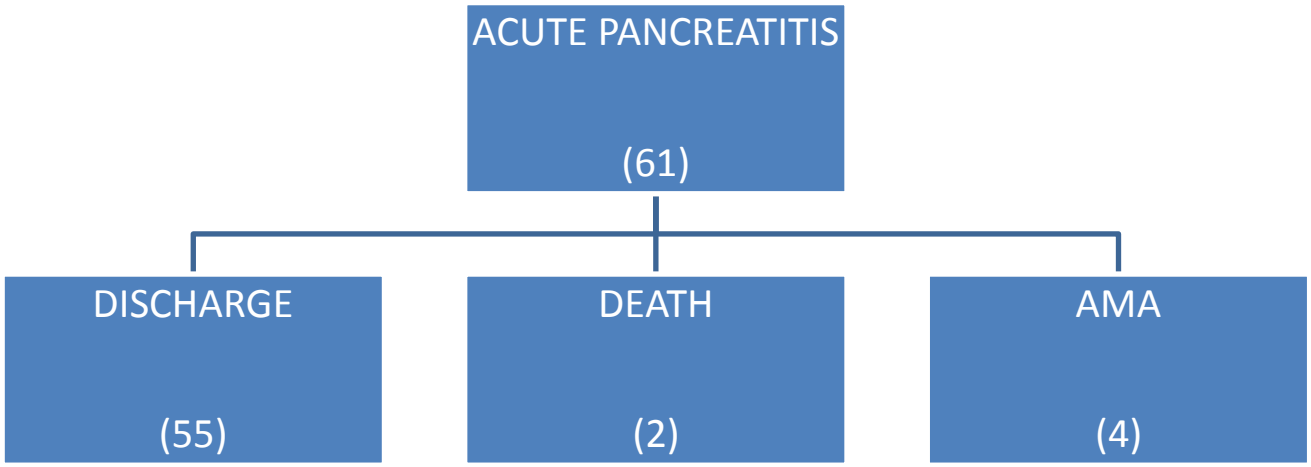
4-6: Moderate Acute Pancreatitis

7-10: Severe Acute Pancreatitis

ANALYSIS AND OBSERVATIONS:

The study included 61 patients with Acute Pancreatitis. They were followed up till discharge, death or AMA. Demographics like age and gender were analysed using simple statistics like proportions.

A schematic representation of the study is shown below :



1.GENDER DISTRIBUTION

TABLE NO. 6

SEX	MALE	FEMALE
No.	51	10

This Table shows the Gender Distribution among the patients. 51 of them were males and 10 of them were females indicating a male predominance. The ratio seems to be 5.1:1 in favour of males.

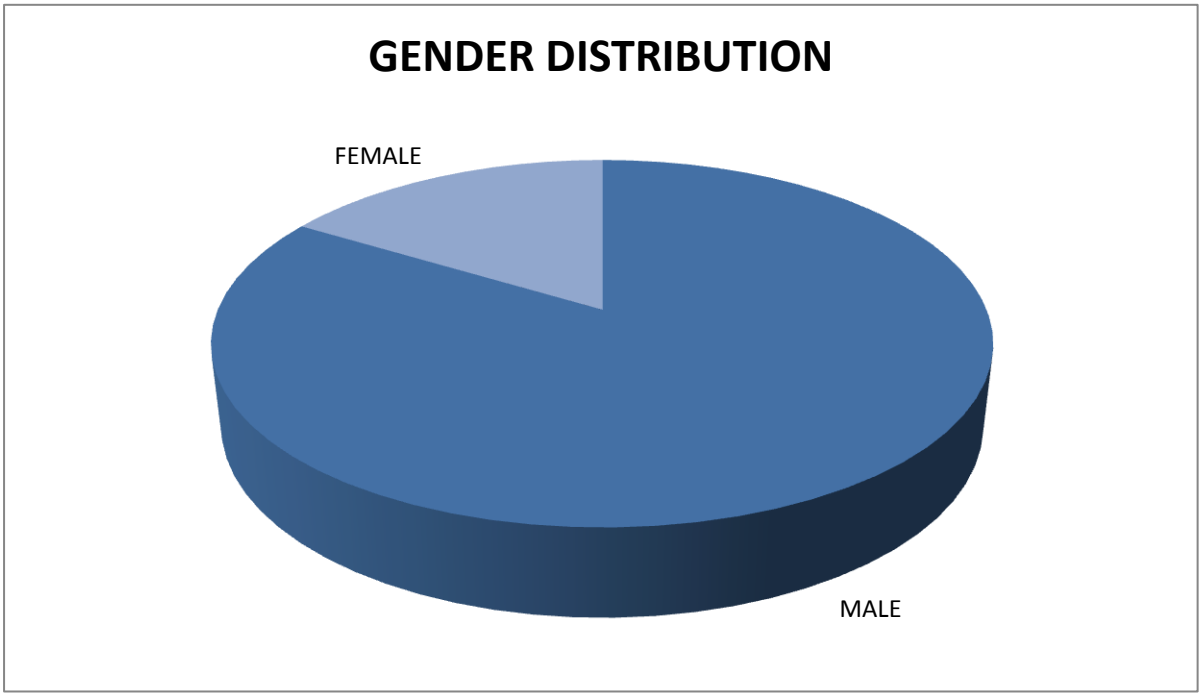


FIGURE 1 SHOWS GENDER DISTRIBUTION

2.AGE DISTRIBUTION

TABLE NO. 7

Range	18-30	31-45	46-60	61-75	Total
Number	7	29	21	4	61

This Table shows the Age distribution among the patients showing a predominance among the age groups 31-45 and 46-60.

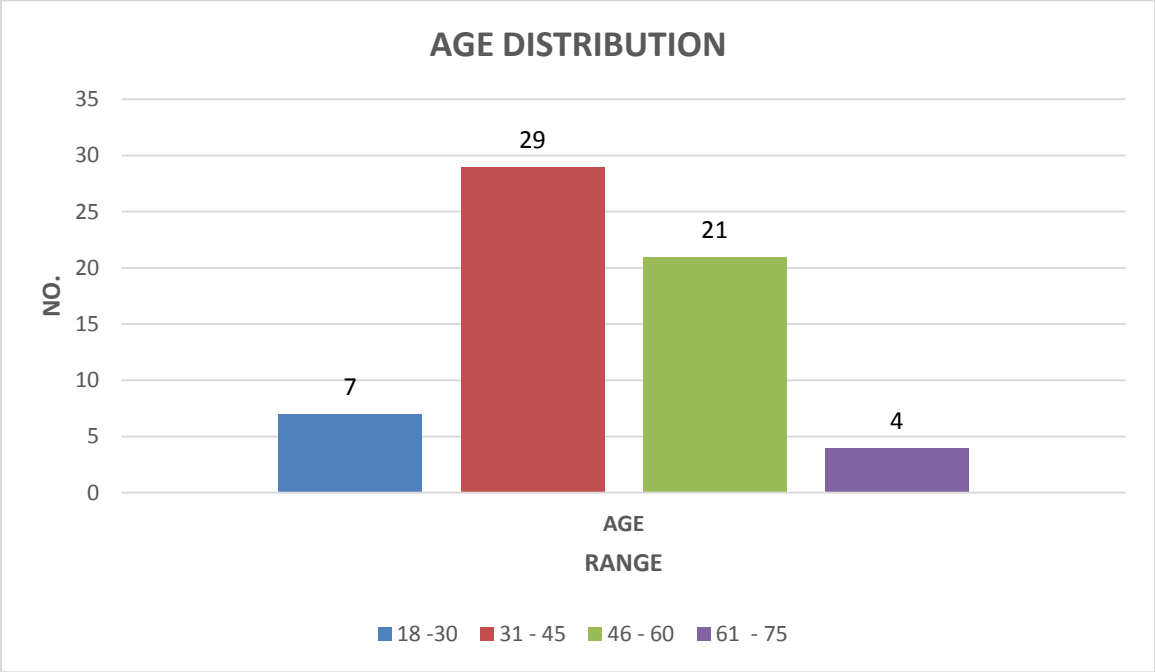


FIGURE 2 AGE DISTRIBUTION

2.A.AGE DISTRIBUTION AMONG MALES
TABLE NO. 8

Range	18-30	31-45	46-60	61-75	Total
Male	7	22	18	4	51

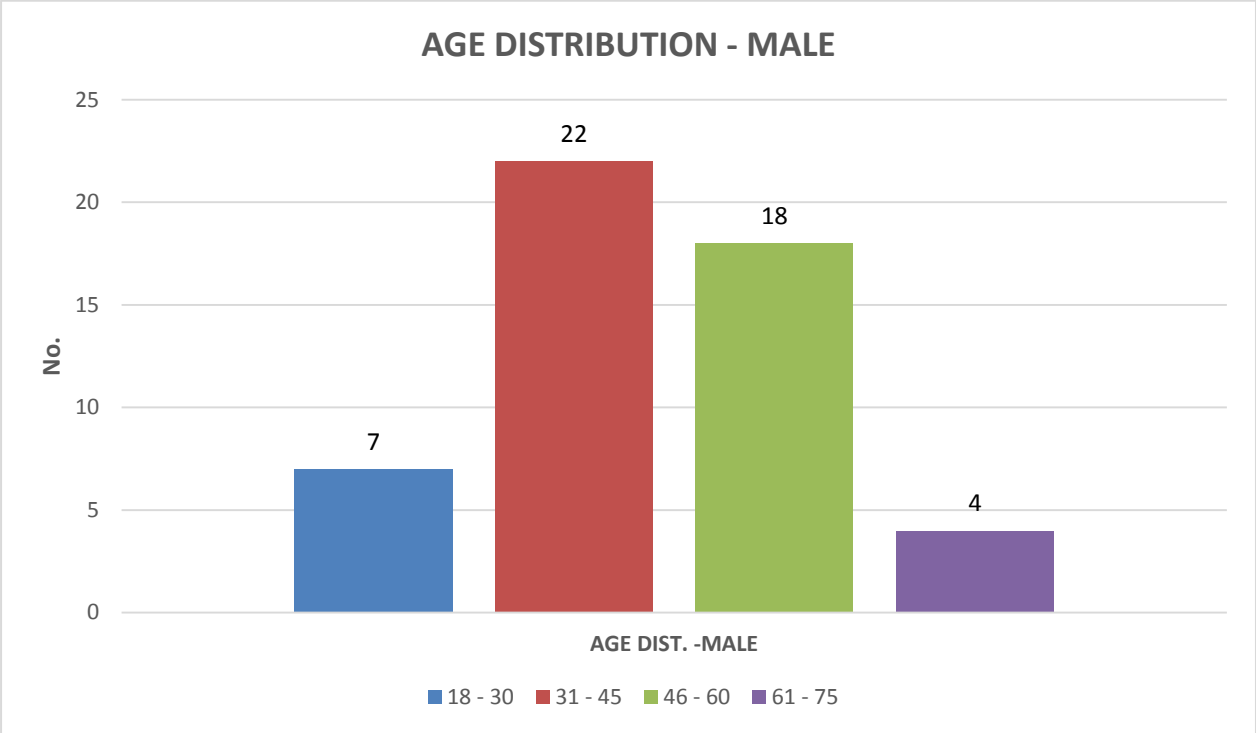


FIGURE 3 AGE DISTRIBUTION AMONG MALES

2.B.AGE DISTRIBUTION AMONG FEMALES

TABLE NO. 9

Range	18-30	31-45	46-60	61-75	Total
Female	0	7	3	0	10

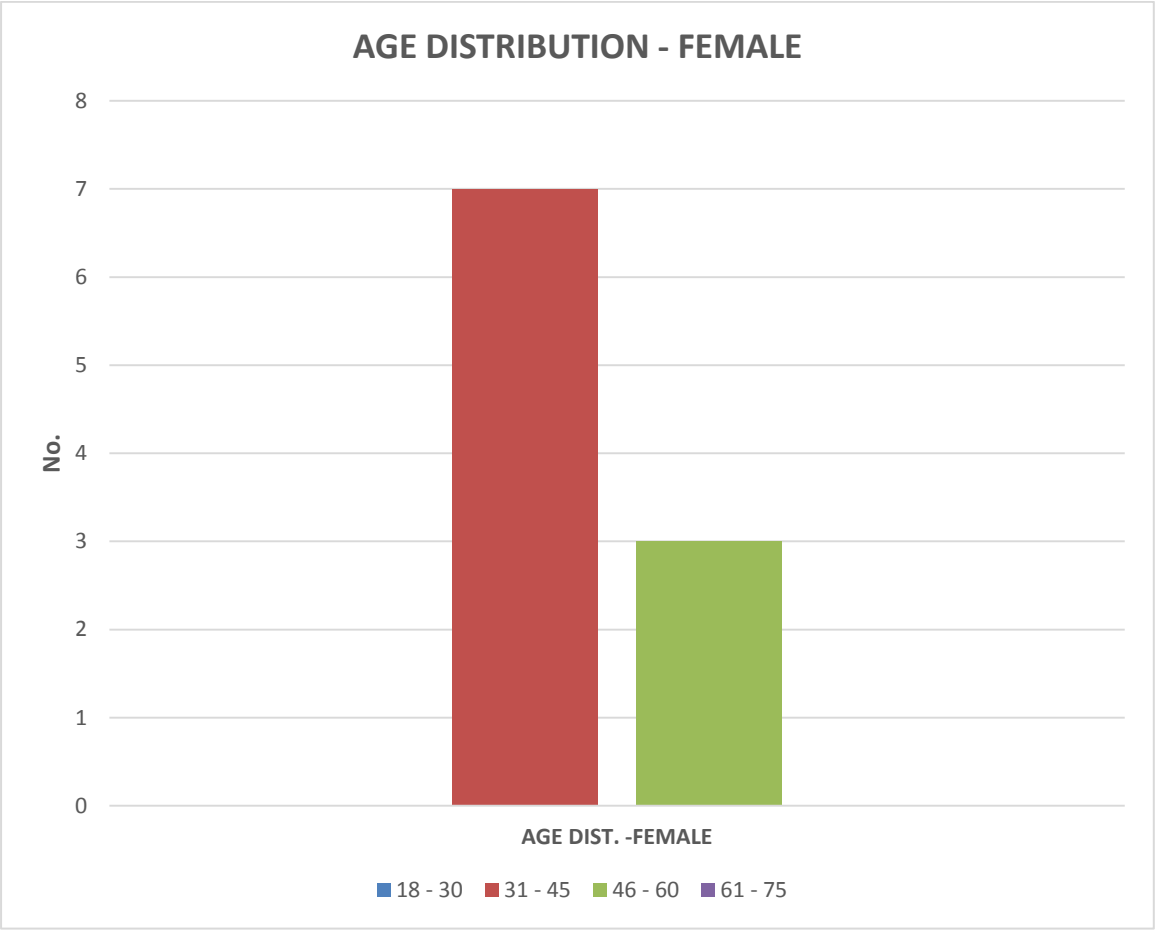


Figure 4 AGE DISTRIBUTION AMONG FEMALES

2 .C.GENDER DISTRIBUTION AMONG THE AGE GROUP 18-30YRS

TABLE NO. 10

Sex/Age	18-30
Male	7
Female	0

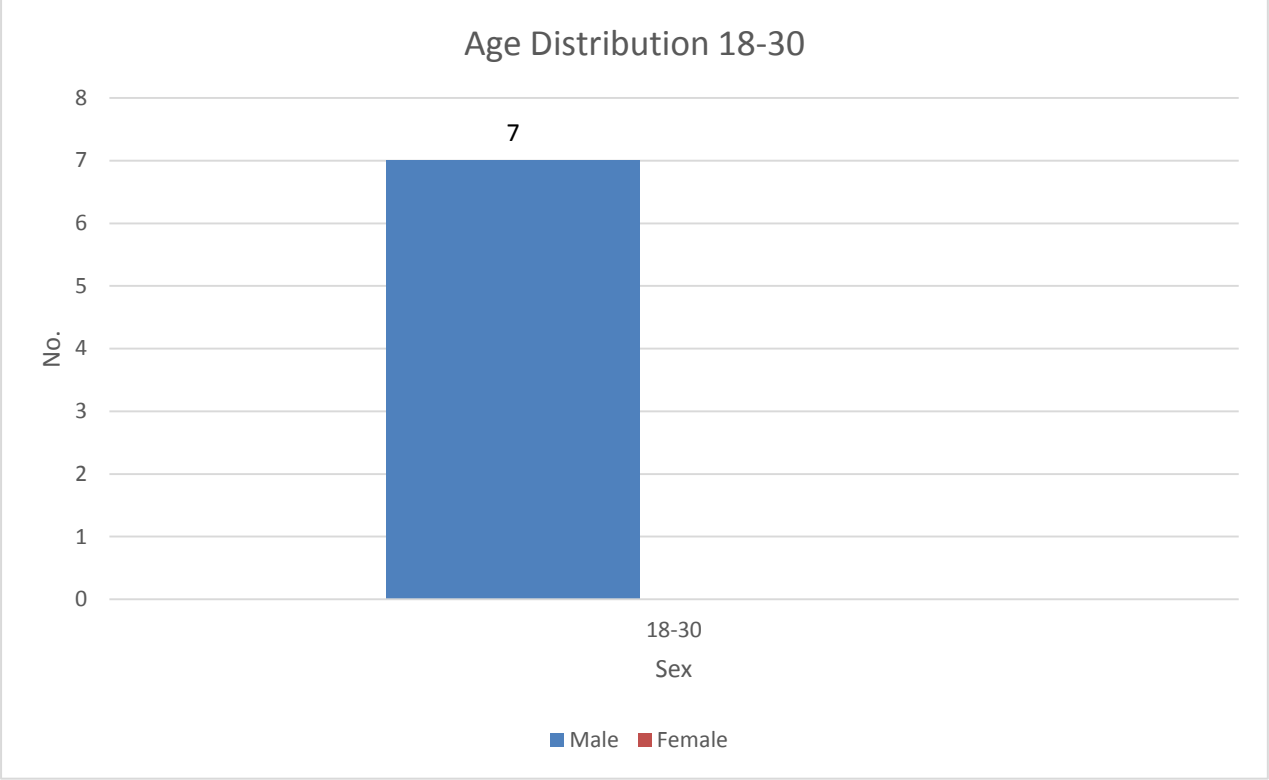


FIGURE5 SEX DISTRIBUTION B/W AGE 18-30 YRS

2.D.GENDER DISTRIBUTION AMONG THE AGE GROUP 31-45YRS

TABLE NO. 11

Sex/Age	31-45
Male	22
Female	7

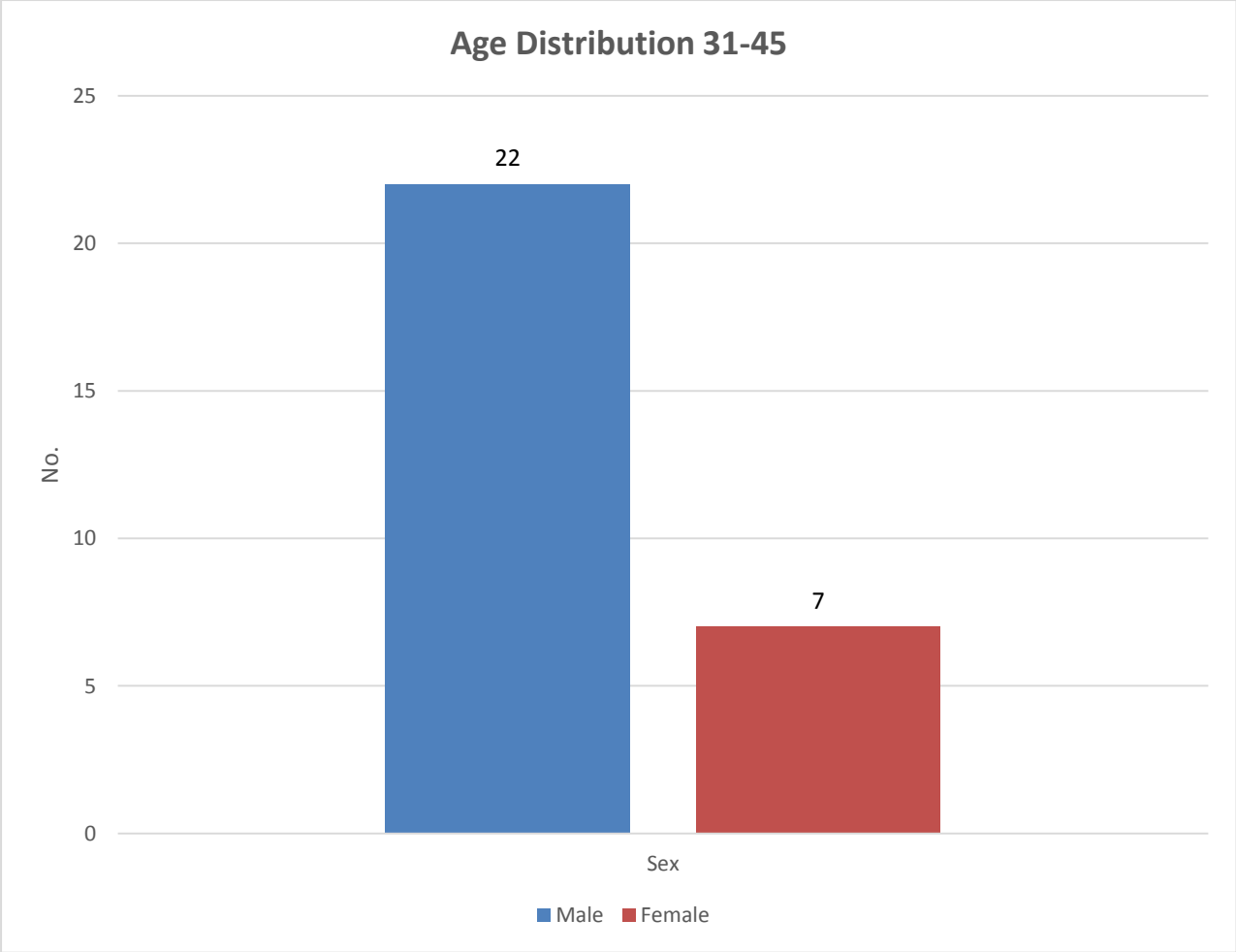


FIGURE 6 SEX DISTRIBUTION B/W AGE 31- 45YRS

2.E.GENDER DISTRIBUTION AMONG THE AGE GROUP 46-60 YRS

TABLE NO. 12

Sex/Age	46-60
Male	18
Female	3

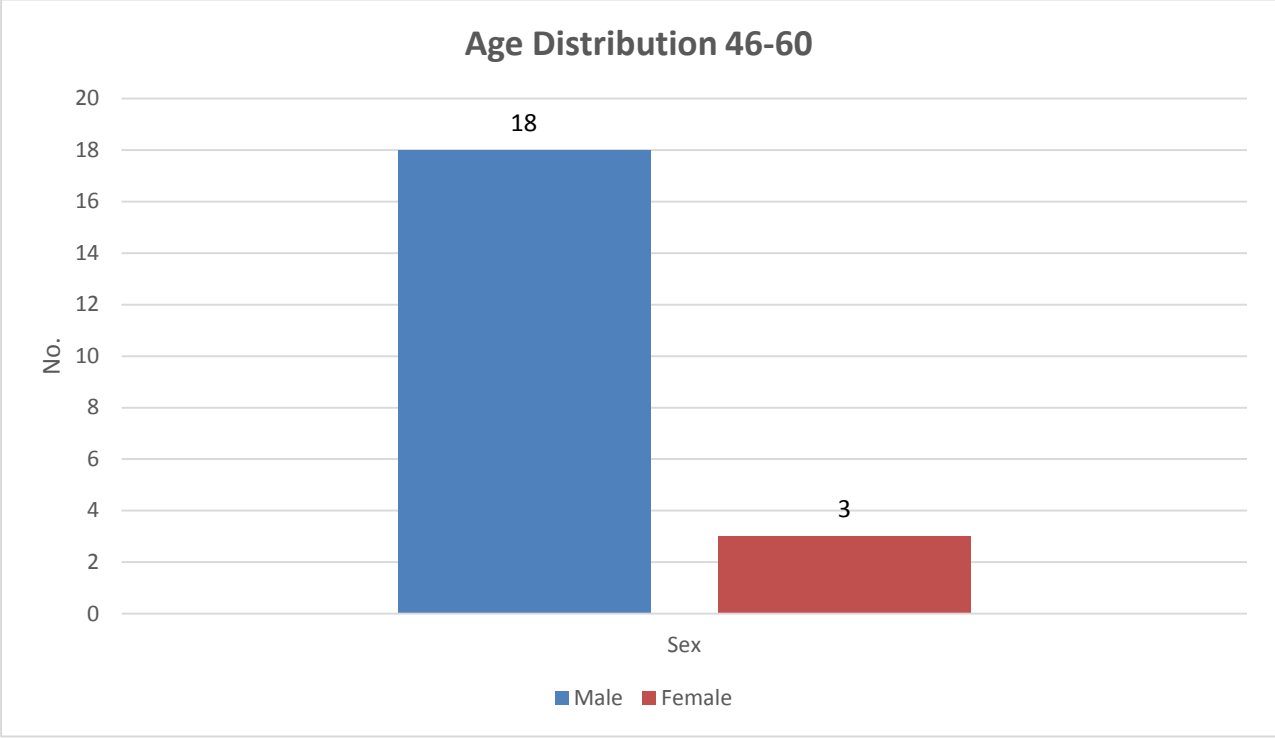


FIGURE 7 SEX DISTRIBUTION B/W AGE 46-60YRS

2.F.GENDER DISTRIBUTION AMONG THE AGE GROUP 61-75 YRS

TABLE NO. 13

Sex/Age	61-75
Male	4
Female	0

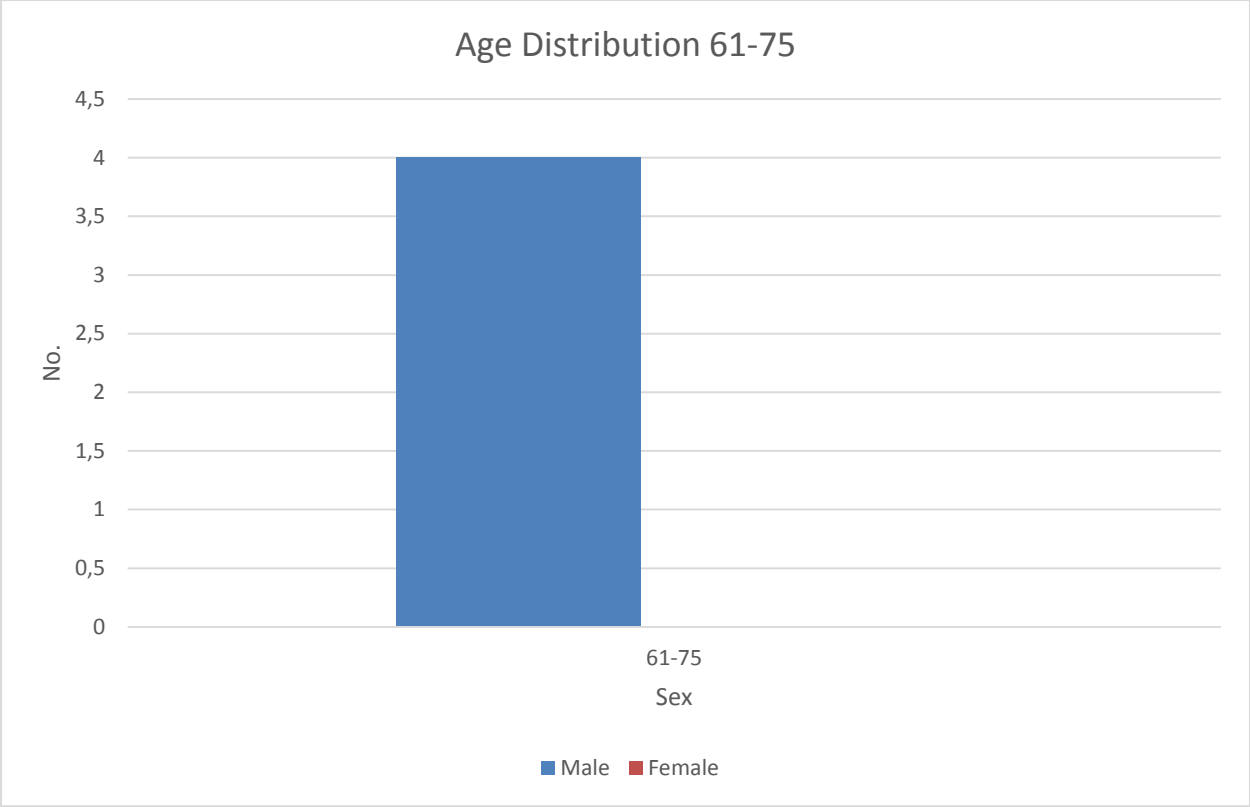


FIGURE 8 SEX DISTRIBUTION B/W AGE 61-75

3. PROGNOSIS

TABLE NO. 14

PROGNOSIS	DISCHARGE	DEATH	AMA	TOTAL
No.	55	2	4	61

This table shows the prognosis of the patients under study. 55 patients comprising the majority of the patients were discharged showing that acute pancreatitis predominantly manifests mildly. However 2 patients expired and 4 went under AMA.

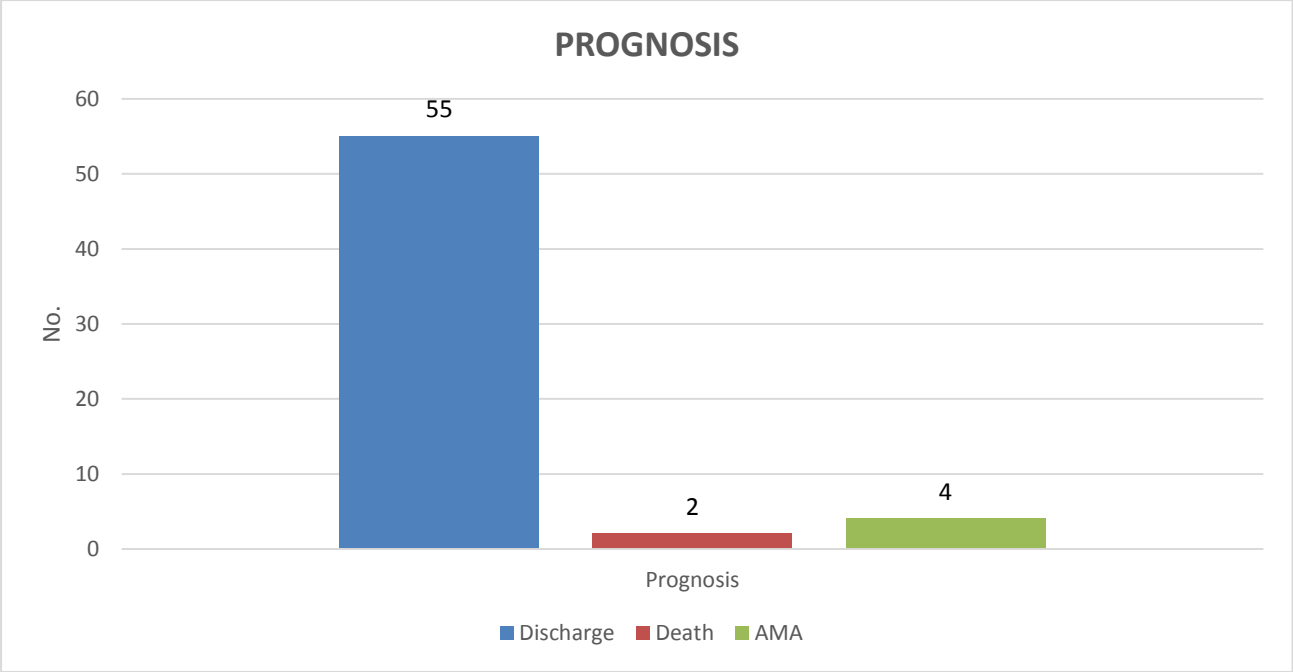


FIGURE 9 PROGNOSIS

4.RANSON CRITERIA

TABLE NO. 15

Ranson	Mild	Moderate	Total
No.	43	18	61

This table shows the distribution of the results of Ransons Criteria when applied to the 61 patients. The majority of them were Mild and 18 were moderate.

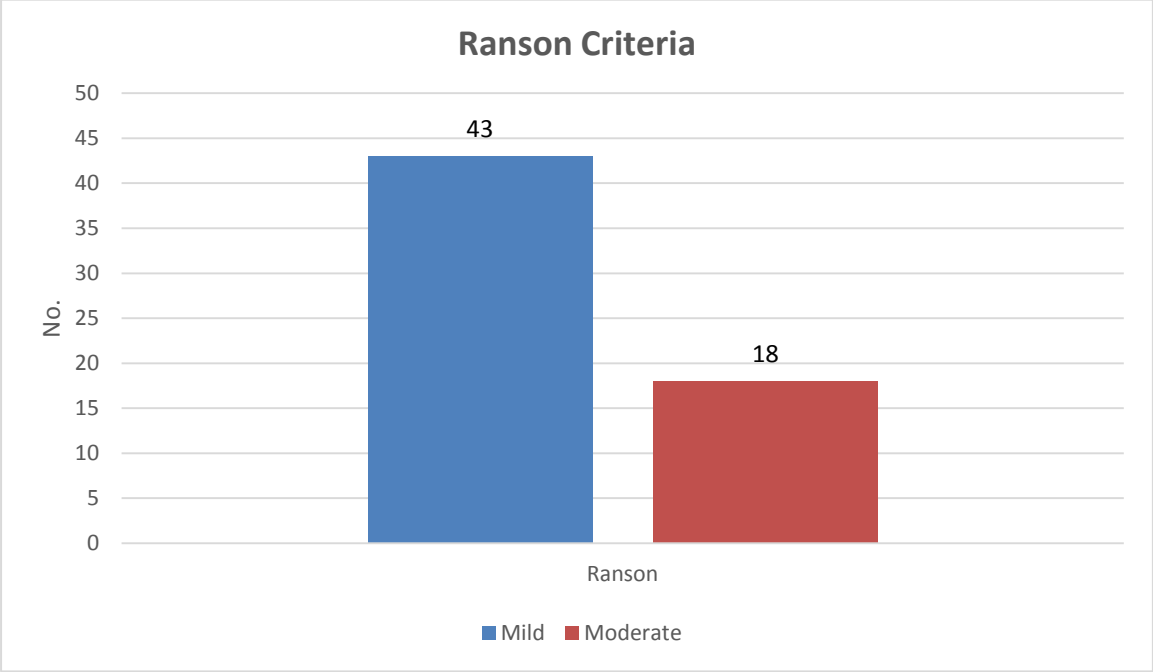


FIGURE 10 RANSON'S CRITERIA

5. CT SEVERITY INDEX

TABLE NO. 16

Severity	Mild	Moderate	Total
No.	42	19	61

This table shows the distribution of the results of Balthazar Scoring when applied to the 61 patients. This also shows the predominance of Mild nature of the Disease.

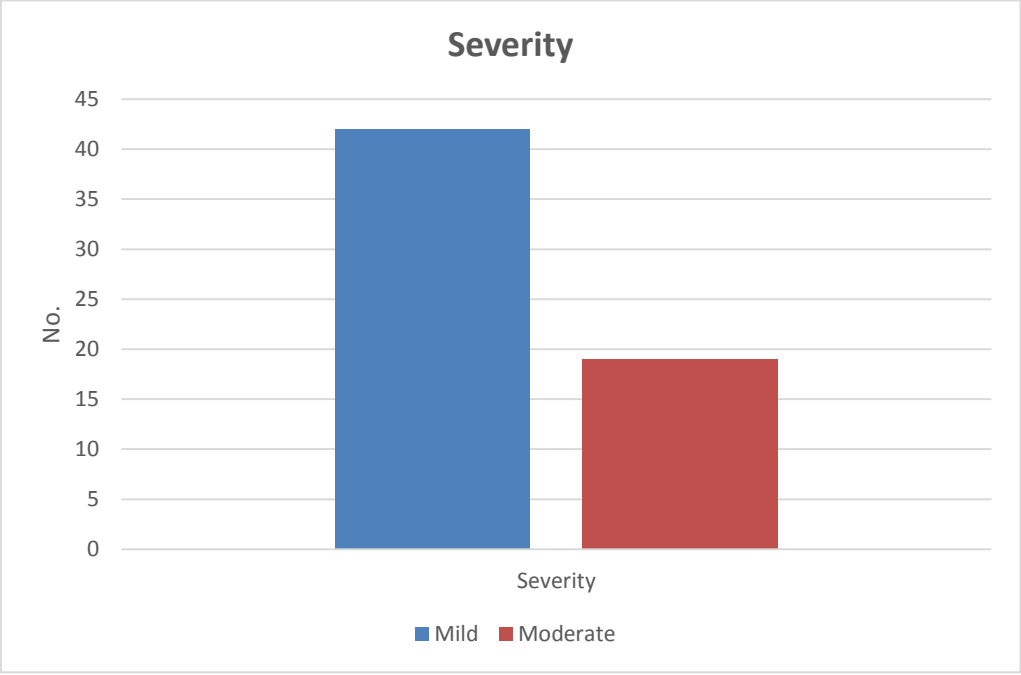


Figure 11 CT SEVERITY INDEX

6. MODS SEVERITY SCORE

TABLE NO. 17

MODS	GRADE 1	GRADE 2	Total
No.	48	13	61

This table shows the distribution of the results of MODS Scoring when applied to the 61 patients. This also shows a predominance of Mild nature of the Disease.

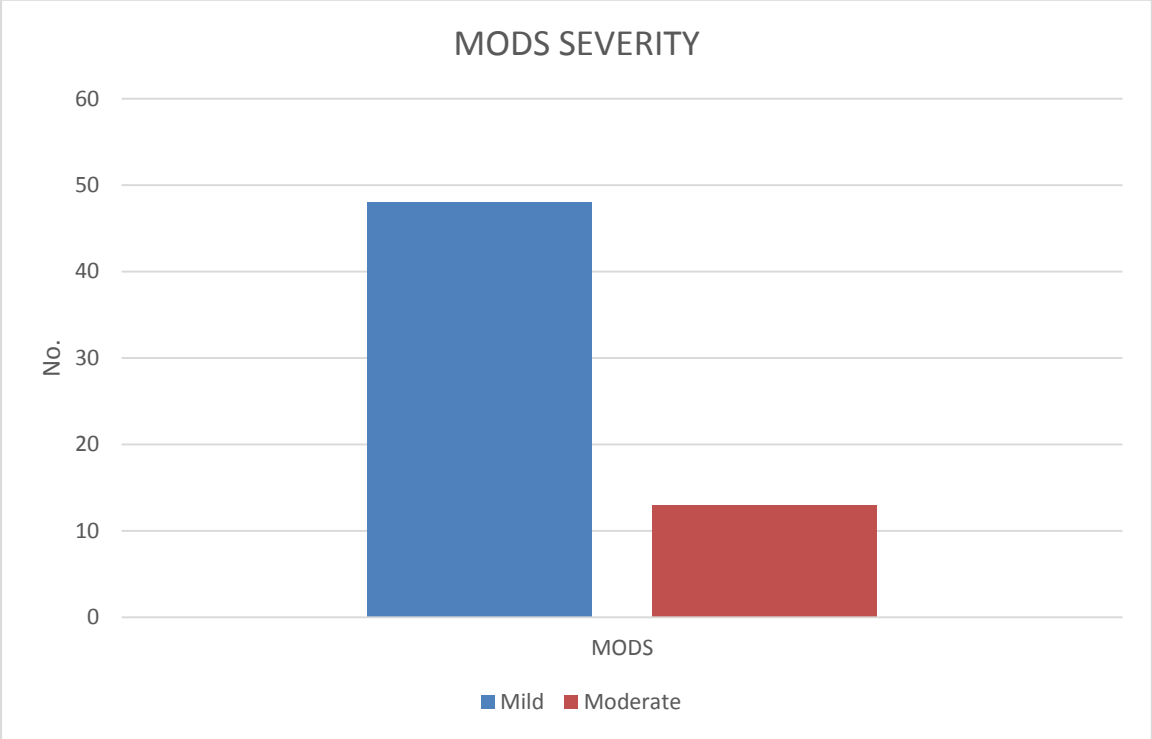


Figure 12 MODS SEVERITY

7. DURATION OF STAY

TABLE NO. 18

DAYS	1-10	11-20	21-30	TOTAL
NO.	42	16	3	61

This Table shows the distribution of duration of stay among the patients includeng expired and AMA patients. Majority of the patients were discharged within 10 days.

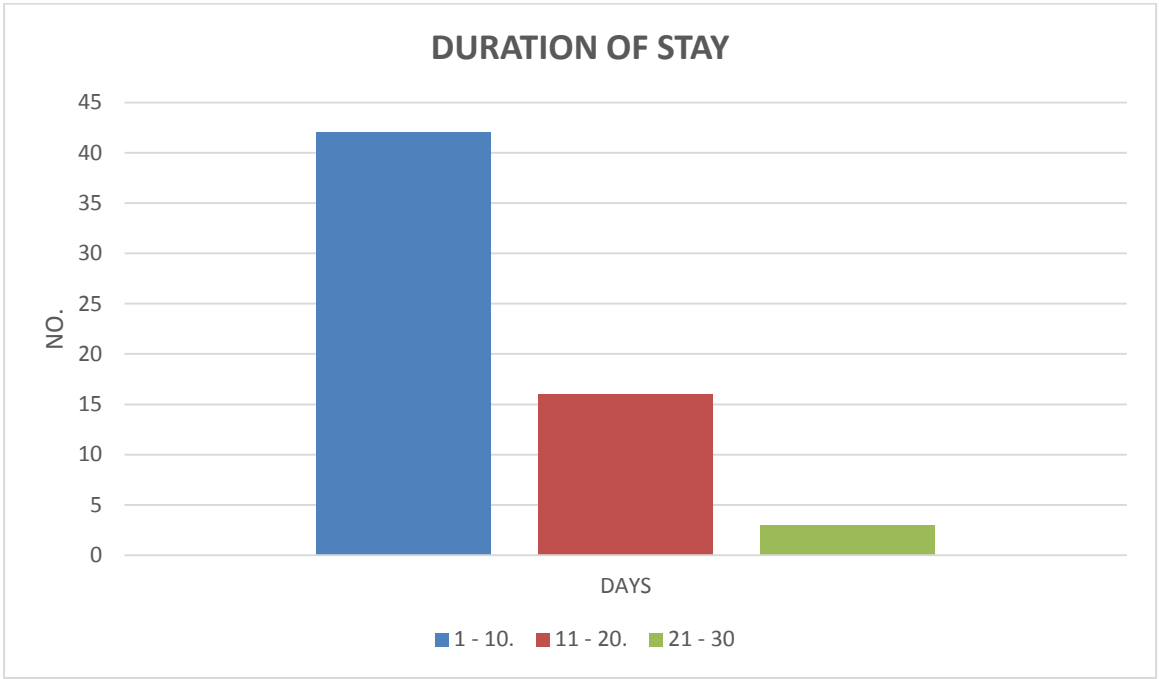


Figure 12 DURATION OF STAY

8. SIGNIFICANCE OF RANSONS CRITERIA AGAINST PROGNOSIS

TABLE NO. 19

		Prognosis			Total
		Discharge	**Death**	**AMA**	
Ransons criteria	Mild	41	0	2	43
	Mod	14	2	2	18
Total		**55**	**2**	**4**	**61**

Statistically Significant p=0.049

This shows that Ransons Criteria accurately predicts the prognosis of the patient.

9. SIGNIFICANCE OF CT SEVERITY INDEX AGAINST PROGNOSIS

TABLE NO. 20

		Prognosis			Total
		Discharge	**Death**	**AMA**	
CT Severity Index	Mild	41	0	1	42
	Mod	14	2	3	19
Total		**55**	**2**	**4**	**61**

Statistically Significant p=0.012,

This shows that CT severity Index accurately predicts the outcome of the disease.

MODS VS CT SEVERITY INDEX

TABLE NO. 21

MODS severity * CT severity index Crosstabulation

			CT severity index		Total
			1.00	2.00	
MODS severity	2.00	Count	39	9	48
		% within severity index	92.9%	47.4%	78.7%
	3.00	Count	3	10	13
		% within severity index	7.1%	52.6%	21.3%
Total		Count	42	19	61
		% within severity index	100.0%	100.0%	100.0%

p=0.000

This tables shows the correlation between MODS and CT severity . It indicates that there is perfect correlation between both which was the aim of this study.

RANSON VS SEVERITY INDEX

TABLE NO. 22

RANSONS CRITERIA * CT severity index Crosstabulation

			Severity Index		Total
			1.00	2.00	
Ranson	1.00	Count	41	2	43
		% within severity index	97.6%	10.5%	70.5%
	2.00	Count	1	17	18
		% within severity index	2.4%	89.5%	29.5%
Total		Count	42	19	61
		% within severity index	100.0%	100.0%	100.0%

P=0.000

This table shows the correlation between Ransons criteria and CT severity index implying the objective of this study.

DISCUSSION

Acute pancreatitis is one of the common gastrointestinal reasons for hospitalisation. Of the 61 patients in this study, 51 were male and 10 were females. Male female ratio in this study was 5.1 : 1. Michael C. Hill et al had 65 males and 37 females in their study. Michael Brand et al also had 63 men and 36 women in their study.

The age group range in this study was 18 to 75 years with majority of patients in the age group of 31 to 45 years. Michael Brand et al in their study also had study population in the age group of 18 to 84 years. In this study, in 18 to 30 age group, only 7 males were there; In 31 to 45 years age group, number of males and females were 22 and 7 respectively; In 46 to 60 years age group number of males and females were 18 and 3 respectively; In 61 to 75 years age group only 4 males were there.

In this study, the severity of acute pancreatitis was graded using both clinical criteria and CT scan. As per Ranson criteria, 43 patients were graded as mild pancreatitis and 18 patients as moderate. According to CT severity index, the disease was categorised as mild and moderate; 42 patients were under mild and 19 patients under moderate category. Michael C. Hill et al had 24 patients with normal CT, 51 patients with grade 1 or 2 pancreatitis and 16 patients with grade 3 or 4 pancreatitis.

In this study, the number of patients with grade 1 MODS severity score was 48 and with moderate score was 13.

In this study, according to Ranson criteria, among the 43 patients with mild pancreatitis, 41 improved and got discharged; 2 patients went against medical advice and no deaths. Among the 18 patients with moderate pancreatitis, 14 got improved, 2 patients went out against medical advice and 2 patients died.

According to CT severity scoring, among the 42 patients with mild pancreatitis, 41 got discharged and 1 went against medical advice; among 19 patients with moderate score, 14 got improved, 2 patients died and 3 patients went out against medical advice.

Among the 61 patients, 48 were under grade 1 MODS severity score of which 45 got discharged, 1 patient expired and 2 went against medical advice; 10 were under grade 2 score of which 10 got discharged, 1 patient died and 2 patients went against medical advice.

The mean duration of stay in hospital was 9.7 ± 4.73 days. Majority of patients had a hospital stay for 1 to 10 days (42 patients) followed by 11 to 20 days (16 patients) and 3 days (21 to 30 patients). When the duration of stay was compared among the survivors and non survivors, the mean duration of stay among survivors is 10 days and among non survivors is 9.5 ± 3.5 days.

Comparison between the Ranson score and CT severity score was made. As per Ranson score, 43 (70.5%) patients were found to be in mild category and 18 (29.5%) were in moderate category. According to CT severity sore, 42 (68.85%) were in mild category and 19 (31.14%) patients were in moderate category.

Comparison MODS score and CT severity score was made. As per MODS score, 48 (78.7%) patients were in grade 1and 13 (21.3%) were in grade 2. According to CT severity score, 42 and 19 patients were in mild and moderate category respectively.

Of the total 61 patients, 55 patients got discharged, 2 patients expired and 4 patients went out against medical advice.

CONCLUSION

1. There is a correlation between CT Severity Index and Ransons Criteria which signifies the aim of the study.
2. Also there is a correlation between CT Severity Index and Prognosis of the patient implying that CT plays a critical role in initial process of diagnoses, as an early predictive indicator of disease severity, and in detecting complications associated with acute pancreatitis.
3. CT is an important single imaging modality to evaluate patients with acute pancreatitis.
4. CT has a high sensitivity and specificity in diagnoses of moderate and severe forms of pancreatitis and it is used to confirm clinical diagnosis as well as to detect other intra-abdominal catastrophes that may mimic acute pancreatitis.
5. Early CT evaluation allows identification of group of patients at high risk of local complications. These group of patients should be followed up with serial CT examinations and should be monitored closely.

CASE PROFORMA

NAME:

AGE:

IP NUMBER:

UNIT:

DATE OF ADMISSION: COMPLAINTS:

GENERAL EXAMINATION:

GCS: SPO2: BP: PR:

RESPIRATORY RATE:

TEMPERATURE:

SYSTEMIC EXAMINATION: INVESTIGATIONS:

SERUM AMYLASE:

RANSON CRITERIA**:**

ATADMISSION: **CRITERIA** **SCORE**

AGE:

BLOOD GLUCOSE: WCC:

LDH:

SGOT:

48 HRS AFTER ADMISSION:

HEMATOCRIT DECREASE: SERUM UREA

INCREASE: SERUM CALCIUM:

FLUID SEQUESTRATION: SPO2:

BASE DEFICIT:

MODS SCORE**:**

ORGANSYSTEMS SCORE

Respiratory:

Renal:

Hepatic:

Cardiovascular:

Central nervous system: Hematological:

USG ABDOMEN: CT ABDOMEN:

UNENHANCED CTSCORE: Grade: Score:

Necrosis index:
Severity index:

BIBLIOGRAPHY

1. Effrey B. Matthews, MD., Shackelford's Surgery Alimentary Tract

2. haheen NJ, Hansen RA, Morgan DR, et al: The burden of gastrointestinal and liver diseases, 2006. *Am J Gastroenterol*,2006.

3. Banks PA, Freeman ML: Practice guidelines in acute pancreatitis. *Am J Gastroenterol*, 2006.

4. Besselink MG, Van Santvoort HC, Boermeester MA, et al: Timing and impact of infections in acute pancreatitis. *Br J Surg*, 2009.

5. UK guidelines for the management of acute pancreatitis. *Gut* , 2005.

6. Petrov MS, Shanbhag S, Chakraborty M, et al: Organ failure and infection of pancreatic necrosis as determinants of mortality in patients with acute pancreatitis. *Gastroenterology*, 2010.

7. Mao EQ, Tang YQ, Fei J, et al: Fluid therapy for severe acute pancreatitis in acute response stage. *Chin Med J (Engl)*, 2009.

8. Van Santvoort HC, Besselink MG, Bakker OJ, et al: A step-up approach or open necrosectomy for necrotizing pancreatitis. *N Engl J Med*, 2010.

9. Eckerwall GE, Tingstedt BB, Bergenzaun PE, et al: Immediate oral feeding in patients with mild acute pancreatitis is safe and may accelerate recovery: A randomized clinical study. *Clin Nutr*, 2007.

10. Petrov MS, Zagainov VE. Influence of enteral versus parenteral nutrition on blood glucose control in acute pancreatitis: A systematic review. *Clin Nutr*, 2007.

11. Petrov MS, Loveday BP, Pylypchuk RD, et al: Systematic review and meta-analysis of enteral nutrition formulations in acute pancreatitis. *Br J*, 2009.

12. De Vries AC, Besselink MGH, Van der Kraats CIB, et al: Antibiotic prophylaxis in acute necrotizing pancreatitis: Methodological quality of randomised controlled trials in relation to outcome. *Gut*, 2005.

13. Wittau M, Mayer B, Scheele J, et al: Systematic review and metaanalysis of antibiotic prophylaxis in severe acute pancreatitis. *Scand J Gastroenterol*, 2011.

14. Luiten EJ, Hop WC, Lange JF, et al: Controlled clinical trial of selective decontamination for the treatment of severe acute pancreatitis. *Ann Surg*, 1995.

15. Van Santvoort HC, Besselink MG, Timmerman HM, et al: Probiotics in surgery. *Surgery*, 2008.

16. Mier J, Luque-de León E, Castillo A, et al: Early versus late necrosectomy in severe necrotizing pancreatitis. *Am J Surg*, 1997.

17. Cheatham ML, Malbrain ML, Kirkpatrick A, et al: Results from the International Conference of Experts on Intra-abdominal Hypertension and Abdominal Compartment Syndrome. II. Recommendations *Intensive Care Med*, 2007.

18. 18. Besselink MG, Van Santvoort HC, Bakker OJ, et al: Draining sterile fluid collections in acute pancreatitis? Primum non nocere! *Surg Endosc*, 2011.

19. Zerem E, Imamovic G, Omerovic S, et al: Randomized controlled trial on sterile fluid collections management in acute pancreatitis: Should they be removed? *Surg Endosc* 2009 May 15.

20. Petrov MS, Van Santvoort HC, Besselink MG, et al: Early endoscopic retrograde cholangiopancreatography versus conservative management in acute biliary pancreatitis without cholangitis: A meta-analysis of randomized trials. *Ann Surg*, 2008.

21. Van Santvoort HC, Besselink MG, De Vries AC, et al: Early endoscopic retrograde cholangiopancreatography in predicted severe acute biliary pancreatitis: A prospective multicenter study. *Ann Surg*, 2009.

22. Besselink MG, Verwer TJ, Schoenmaeckers EJ, et al: Timing of surgical intervention in necrotizing pancreatitis. *Arch Surg*,2007.

23. Van Baal MC, Van Santvoort HC, Bollen TL, et al: Systematic review of percutaneous catheter drainage as primary treatment for necrotizing pancreatitis. *Br J Surg*, 2011.

24. orvath K, Freeny P, Escallon J, et al: Safety and efficacy of videoassisted retroperitoneal debridement for infected pancreatic collections: A multicenter, prospective, single-arm phase 2 study. *Arch Surg*, 2010.

25. Horvath KD, Kao LS, Wherry KL, et al: A technique for laparoscopicassisted percutaneous drainage of infected pancreatic necrosis and pancreatic abscess. *Surg Endosc*, 2001.

26. Van Santvoort HC, Besselink MGH, Horvath KD, et al: Videoscopic assisted retroperitoneal debridement in infected necrotizing pancreatitis. *HPB (Oxford)*, 2007.

27. Raraty MG, Halloran CM, Dodd S, et al: Minimal access retroperitoneal pancreatic necrosectomy: Improvement in morbidity and mortality with a less invasive approach. *Ann Surg*, 2010.

28. Papachristou GI, Takahashi N, Chahal P, et al: Peroral endoscopic drainage/debridement of walled-off pancreatic necrosis. *Ann Surg* 245:943, 2007.

29. Seifert H, Biermer M, Schmitt W, et al: Transluminal endoscopic necrosectomy after acute pancreatitis: A multicentre study with long-term follow-up (the GEPARD Study). *Gut*, 2009.

30. Voermans RP, Bruno MJ, van Berge Henegouwen MI, et al: Review article: Transluminal endoscopic debridement of organized pancreatic necrosis—the first step towards natural orifice transluminal endoscopic surgery. *Aliment Pharmacol Ther*, 2007.

31. Besselink MG, De Bruijn MT, Rutten JP, et al: Surgical intervention in patients with necrotizing pancreatitis. *Br J Surg*, 2006.

32. Rau B, Bothe A, Beger HG. Surgical treatment of necrotizing pancreatitis by necrosectomy and closed lavage: Changing patient characteristics and outcome in a 19-year, single-center series. *Surgery*, 2005.

33. Rodriguez JR, Razo AO, Targarona J, et al: Debridement and closed packing for sterile or infected necrotizing pancreatitis: Insights into indications and outcomes in 167 patients. *Ann Surg*, 2008.

34. Nealon WH, Bawduniak J, Walser EM. Appropriate timing of cholecystectomy in patients who present with moderate to severe gallstone-associated acute pancreatitis with peripancreatic fluid collections. *Ann Surg*, 2004.

INFORMATION SHEET

Place of Study **:** Chengalpattu Medical College Hospital

Name of the Investigator: Dr. Prashanth Venkatesan

Name of the Participant : **Age:** **Hospital No:**

We are conducting a study on "**CLINICAL AND RADIOLOGICAL CORRELATION OF SEVERITY OF ACUTE PANCREATITIS**" The purpose of the study is to look for the correlation between clinical and radiological grading of severity of Acute Pancreatitis in patients in Chengalpattu Medical College Hospital – Chengalpattu.

The privacy of the patient in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research , no personally identifiable information will be shared.

Taking part in the study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time. Your decision will not result in any loss of benefits to which you are otherwise entitled.

- The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

- You are invited to take part in this study. The information in the document is meant to help you decide whether or not to take part . Please feel free to ask if you have any queries or concerns.
- We have obtained approval from the institutional ethical committee

PRINCIPAL INVESTIGATOR

DR. PRASHANTH VENKATESAN

Final year MS post graduate student,

Department of General Surgery,

Chengalpattu Medical College, Chengalpattu.

Signature of investigator **Signature of patient /guardian**

Date :

Chengalpattu

INFORMED CONSENT FORM

Title of the Study : "**CLINICAL AND RADIOLOGICAL CORRELATION OF SEVERITY OF ACUTE PANCREATITIS**".

Name of the Participant :

_____

_____.

Name of the Principal (Co-Investigator) :

_____.

Name of the Institution : Government Chengalpattu Medical College and Hospital

Name and address of the sponsor / agency(ies) (If any) :

_____

_____

_____

Documentation of the informed consent :

I _____have read the information in this form (or it has been read to me). I was free to ask any questions and they have been answered. I am over 18 years of age and, exercising my free power of choice, hereby give my consent to be included as a participant in "**CLINICAL AND RADIOLOGICAL CORRELATION OF SEVERITY OF ACUTE PANCREATITIS**" (title of the study).

1. I have read and understood this consent form and the information provided to me.
2. I have had the consent document explained to me.
3. I have been explained about the nature of the study.
4. I have been explained about my rights and responsibilities by the investigator.
5. I have been informed the investigator of all the treatments I am taking or have taken in the past _____ months including any native (alternative) treatment.
6. I have been advised about the risks associated with my participation in this study.*
7. I agree to cooperate with the investigator and I will inform him/her immediately if I suffer unusual symptoms.*
8. I have not participated in any research study within the past _____month(s).*
9. I have not donated blood within the past _____months----add if the study involves extensive blood sampling.*
10. I am aware of the fact that I can opt out of the study at any time without having to give any reason and this will not affect my future treatment in this hospital.*
11. I am also aware that the investigator may terminate my participation in the study at any time, for any reason, without my consent.

12. I hereby give permission to the investigators to release the information obtained from me as result of participation in this study to the sponsors, regulatory authorities, Govt. agencies, and IEC. I understand that they are publicly presented.
13. I have understand that my identity will be kept confidential if my data are publicly presented .
14. I have had my questions answered to my satisfaction.
15. I have decided to be in the research study.

I am aware that if I have any question during this study, I should contact the investigator. By signing this consent form I attest that the information given in this document has been clearly explained to me and understood by me, I will be given a copy of this consent document.

SIGNATURE

MASTER CHART

S.NO.	NAME	AGE	SEX	IP NO.	DOA	DOD/AMA/EXPIRED		Outcome grading 1 - improved; 2 - death; 3 - AMA	RANSONS CRITERIA	Ransons score 1 - 0 to 2; 2 - 3 to 4; 3 – 5 & more	MODS SCORE	MODS severity score 1 - 0; 2 - 1 to 4; 3 - 5 to 8	CT GRADE	NECROSIS INDEX	SEVERITY INDEX	Severity index score 1 - 0 to 3; 2 - 4 to 6: 3 - 7 to 10	DURATION OF STAY
1	MADHANRAJ	26	M	49373	8/30/2017	9/5/2017	D	1	0	1	2	2	B-1	0	1	1	6
2	AMALA	39	F	49355	8/29/2017	9/7/2017	D	1	3	2	5	3	D-3	2	5	2	9
3	YASIN	28	M	49290	8/27/2017	9/17/2017	D	1	1	1	3	2	B-1	0	1	1	21
4	MUNIYAN	55	M	49262	8/26/2017	9/8/2017	D	1	3	2	6	3	C-2	2	4	2	13
5	KASIYAMMAL	40	F	49190	8/24/2017	9/2/2017	D	1	2	1	5	3	C-2	0	2	1	9
6	LAKSHMAN	38	M	48132	8/22/2017	8/29/2017	D	1	1	1	1	2	B-1	0	1	1	7
7	SEKAR	50	M	48086	8/20/2017	8/27/2017	D	1	1	1	1	2	B-1	0	1	1	7
8	SIVA	32	M	47981	8/20/2017	8/29/2017	D	1	1	1	3	2	B-1	0	1	1	9
9	PRABHU	36	M	47707	8/19/2017	8/27/2017	D	1	3	2	2	2	C-2	2	4	2	8
10	NAGARAJ	51	M	47701	8/18/2017	9/2/2017	D	1	1	1	1	2	D-3	0	3	1	15
11	MOHAN DOSS	31	M	47658	8/17/2017	8/26/2017	D	1	0	1	2	2	B-1	0	1	1	9
12	MARI	60	M	47625	8/16/2017	8/23/2017	D	1	1	1	2	2	B-1	0	1	1	7
13	KUMAR	52	M	47647	8/15/2017	8/23/2017	D	1	1	1	2	2	B-1	0	1	1	8
14	RAMANI	33	F	47299	8/14/2017	8/26/2017	D	1	1	1	2	2	B-1	0	1	1	12
15	LAKSHMI	40	M	46730	8/13/2017	8/20/2017	D	1	2	1	4	2	C-2	1	3	1	7
16	NAVEENKUMAR	35	M	46728	8/12/2017	8/20/2017	D	1	2	1	3	2	C-2	1	3	1	8
17	MARIYASELVAM	43	M	46670	8/11/2017	8/21/2017	D	1	1	1	2	2	B-1	0	1	1	10
18	RAMESH KUMAR	40	M	46672	8/10/2017	8/24/2017	D	1	2	1	2	2	B-1	0	1	1	14
19	KAMARAJ	45	M	46026	8/9/2017	8/18/2017	D	1	2	1	3	2	C-2	0	2	1	9
20	BASKAR	30	M	45897	8/4/2017	8/15/2017	D	1	4	2	4	2	D-3	1	4	2	11
21	VELU	42	M	45856	7/30/2017	8/22/2017	D	1	4	2	5	3	D-3	1	4	2	23
22	SRINIVASAN	32	M	45783	7/29/2017	8/6/2017	A	3	3	2	5	3	E-4	2	6	2	8
23	SOUNDHARAJAN	60	M	44596	7/28/2017	8/5/2017	D	1	1	1	2	2	B-1	0	1	1	8
24	VENKATESAN	44	M	44318	7/26/2017	8/3/2017	D	1	1	1	2	2	B-1	0	1	1	8
25	KRISHNAVENI	38	F	44312	7/25/2017	8/3/2017	D	1	2	1	3	2	C-2	0	2	1	9
26	MURUGESAN	62	M	44303	7/24/2017	8/20/2017	D	1	2	1	3	2	D-3	1	4	2	27
27	PONNAIYAN	41	M	44280	7/22/2017	8/5/2017	D	1	2	1	2	2	B-1	0	1	1	14
28	SEKAR	56	M	44265	7/19/2017	7/26/2017	D	1	3	2	5	3	D-3	0	3	1	7
29	UMAPATHY	27	M	44270	7/18/2017	7/30/2017	E	2	3	2	4	2	E-4	2	6	2	12
30	ALLAUDIN	32	M	44228	7/17/2017	7/23/2017	D	1	1	1	2	2	B-1	0	1	1	6
31	VIJAYAN	54	M	44154	7/16/2017	7/31/2017	D	1	1	1	2	2	B-1	0	1	1	15
32	MURUGAN	40	M	43690	7/14/2017	7/20/2017	D	1	1	1	3	2	C-2	0	2	1	6
33	RAJENDRAN	55	M	42708	7/13/2017	7/20/2017	A	3	3	2	4	2	D-3	1	4	2	7
34	SUBRAMANI	36	M	42658	7/10/2017	7/17/2017	A	3	2	1	5	3	D-3	1	4	2	7
35	PRABHAKARAN	39	M	42622	7/9/2017	7/15/2017	D	1	2	1	4	2	C-2	0	2	1	6

36	KALIYAMMAL	48	F	42561	7/8/2017	7/16/2017	D	1	1	1	4	2	C-2	0	2	1	8
37	MOHINI	50	F	42564	7/7/2017	7/13/2017	D	1	3	2	5	3	D-3	1	4	2	6
38	ANBHALAGAN	45	M	41608	7/6/2017	7/23/2017	D	1	1	1	4	2	B-1	0	1	1	17
39	CHANDRAN	62	M	41494	7/5/2017	7/12/2017	E	2	3	2	5	3	E-4	1	5	2	7
40	ANNAMALAI	47	M	41178	7/3/2017	7/10/2017	D	1	1	1	2	2	B-1	0	1	1	7
41	SELVAM	49	M	40345	6/30/2017	7/6/2017	D	1	1	1	2	2	B-1	0	1	1	6
42	CHANDRA DEVI	34	F	40628	6/29/2017	7/5/2017	D	1	2	1	4	2	C-2	0	2	1	6
43	RAJESHWARI	60	F	38834	6/28/2017	7/14/2017	D	1	1	1	2	2	B-1	0	1	1	16
44	NEELAKANDAN	49	M	38775	6/27/2017	7/15/2017	D	1	1	1	3	2	C-2	0	2	1	18
45	SIVAKUMAR	47	M	38494	6/27/2017	7/16/2017	D	1	3	2	5	3	E-4	2	6	2	19
46	MURUGESAN	45	M	38430	6/25/2017	7/8/2017	D	1	4	2	4	2	D-3	1	4	2	13
47	VADIVELU	65	M	38432	6/24/2017	7/4/2017	D	1	3	2	5	3	D-3	1	4	2	10
48	SEKAR	53	M	38327	6/21/2017	6/25/2017	D	1	4	2	4	2	E-4	2	6	2	4
49	EGAMBARAM	51	M	36988	6/19/2017	6/25/2017	D	1	0	1	2	2	B(1)	0	1	1	6
50	BALAKRISHNAN	65	M	36989	6/17/2017	6/22/2017	D	1	3	2	5	2	D-3	2	5	2	5
51	SIVA	26	M	36935	6/16/2017	6/24/2017	D	1	1	1	3	2	B-1	0	1	1	8
52	BALAKUMAR	39	M	36903	6/14/2017	6/21/2017	D	1	3	2	6	3	C-2	2	4	2	7
53	MANJULA	35	F	36897	6/13/2017	6/20/2017	D	1	2	1	5	3	C-2	0	2	1	7
54	BASKAR	36	M	36061	6/11/2017	6/24/2017	A	3	1	1	1	2	B-1	0	1	1	13
55	BALASUBRAMANIAM	52	M	35921	6/9/2017	6/18/2017	D	1	1	1	1	2	B-1	0	1	1	9
56	PUSHPA	45	F	35903	6/8/2017	6/13/2017	D	1	1	1	3	2	B-1	0	1	1	5
57	THALAPATHY	25	M	35525	6/6/2017	6/11/2017	D	1	3	2	2	2	C-2	2	4	2	5
58	VIDYAA SAGAR	27	M	35506	6/5/2017	6/12/2017	D	1	1	1	1	2	D-3	0	3	1	7
59	GOKUL	38	M	35494	6/4/2017	6/15/2017	D	1	0	1	2	2	B-1	0	1	1	11
60	GANESAN	47	M	35472	6/3/2017	6/18/2017	D	1	1	1	2	2	B-1	0	1	1	15
61	ARUL VEL	55	M	35442	6/2/2017	6/9/2017	D	1	1	1	2	2	B-1	0	1	1	7